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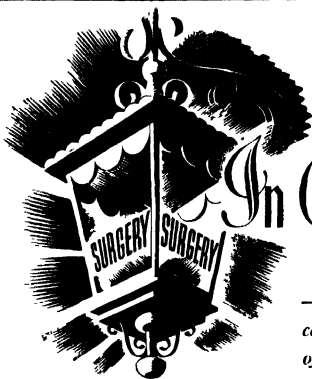
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**THE
BRITISH ENCYCLOPAEDIA
OF MEDICAL PRACTICE**

**SURVEYS AND ABSTRACTS
1940**

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OF MEDICAL PRACTICE**

INCLUDING

**MEDICINE SURGERY
OBSTETRICS GYNAECOLOGY
AND OTHER SPECIAL SUBJECTS**

SURVEYS AND ABSTRACTS

1940

Under the General Editorship of

SIR HUMPHRY ROLLESTON, BT

G.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D.

EMERITUS REGIUS PROFESSOR OF PHYSIC CAMBRIDGE

SOMETIME PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON

Publishing Editor

ADAM CLARK, L.M.S.S.A.

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INTRODUCTION

BY

THE GENERAL EDITOR

As the general plan of the first Annual Supplement to the **BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE** has met with a considerable measure of approval among the subscribers, the same arrangement has been followed in this, the second Annual Supplement. This volume is again divided into three parts, which contain respectively a series of critical surveys of various branches of Medicine, a section dealing with new developments in drugs, and abstracts from current medical literature.

PART I—CRITICAL SURVEYS

This consists of a series of authoritative signed reviews dealing in general terms with the present position of some branches of medical science and practice, and often indicating the possible future developments in these. The subjects dealt with in these critical surveys will vary from year to year according to the circumstances of medical progress. The Encyclopaedia is much indebted for the help given in these difficult times by the contributors of these surveys.

PART II—DRUGS

In this section new drugs, or modifications of old drugs, are discussed from the pharmacological point of view and also from the viewpoint of their application to therapeutics generally.

PART III—ABSTRACTS OF MEDICAL LITERATURE

This section brings together the essentials of a large number of papers published throughout the year by British, American, and foreign authors. In spite of the War, and the resulting disappearance of some medical journals, the output of medical work remains vast, so that the task of presenting a balanced selection, representative of the whole, has not been easy. Much care has, however, been bestowed on the selection of these abstracts which are arranged as far as possible on the same plan as that adopted in the parent Encyclopaedia. The material in this part contains the results and opinions of the authors of the abstracted papers, but it does not, of course, follow that these will be finally accepted by the medical profession.

H.R.

PART I

CRITICAL SURVEYS

GENERAL MEDICINE

BY J. W. McNEE, D.S.O., M.D., D.Sc., F.R.C.P.
REGIUS PROFESSOR OF MEDICINE, UNIVERSITY OF GLASGOW
TEMPORARY SURGEON REAR-ADMIRAL, ROYAL NAVY

The present position and the future of Medicine, as of everything else, are dominated by the impact of the war. All countries in Europe are affected, and the effects must soon be universal.

The stresses and practical necessities of war may act in two ways in Medicine: first, they may narrow down everything to purely practical essentials, working on past knowledge alone and taking no thought for the future. This is what seems, from a perusal of the medical journals, to have happened in Germany within the last two or three years. Second, the magnitude and urgency of practical issues may supply a tremendous stimulus to work, yielding results of importance at once for the health of the contending nations and their fighting services. This was well shown between 1914 and 1918, when the immediate problems of war brought about striking and rapid changes in the treatment of injuries, in knowledge of infections (gas gangrene and anaerobic invasion), and in many other branches of Medicine. This new knowledge passed into civil practice when war ended. Thus, war is always likely to be a powerful stimulus for work yielding practical results, and the hour creates the men to do it.

The sulphonamide compounds

The other development which concerns the present state and the future progress of Medicine is the sudden appearance of the sulphonamide group of drugs, and their beneficial effect on infections of many kinds. What future improvements in this group of drugs may lead to cannot be foreseen, but work goes on at the swiftest pace and will no doubt continue in spite of war. The story of chemotherapy in Medicine is of great interest, especially what may for brevity be termed 'synthetic chemotherapy'. Salvarsan, in 1909, did not represent the actual beginning but was the first outstanding success and raised high hopes of rapid expansion along similar lines. These hopes, however, were not fulfilled, and a lag of over a quarter of a century followed before the advent of the sulphonamide group and the recognition of its anti-streptococcal and other powers.

The common, dangerous, pathogenic organism which still resists attack is the staphylococcus, but it is hoped that some compound such as sulphathiazole may soon prove to be effective against staphylococci in the body tissues.

Serum therapy

It is curious to note how this recent development in chemotherapy bids fair to curtail the domain of serum therapy, in cerebrospinal fever almost certainly, and probably also in pneumonia. Serum therapy clearly has not fulfilled all early expectations, and it may well be that in future the use of antisera will be confined to combating the effects of bacteria which produce exotoxins, as in diphtheria and tetanus.

Vaccine therapy

The decline of vaccine therapy as a means of increasing bodily resistance against microbial infections in the presence of active disease has been gradual but cumulative. In prophylactic medicine (e.g. typhoid fever) it will probably remain, but its failure as a form of active therapy in disease must be evident to all.

Diseases due to viruses

During the last war the vast influenza pandemic of 1917 and 1918 gave the added stimulus, both at the time and ever since, for investigation of diseases due to filter-passing viruses. Included in this group are, among others, influenza, canine distemper, and typhus fever and other rickettsia infections. Much knowledge has been gathered, but, except for the prevention of canine distemper, little of great practical value has so far emerged

Dietetics and deficiency diseases

It is impossible to discuss in any reasonable space the importance of dietetics for the health of the nation in war and peace. It must, however, be recognized that the modern trend of life, with herding in cities, has made great changes in the national diet, and often not for the general good. Even the modern cinema is responsible for an alteration in dietetics; and cooked foods, such as 'fish and chips', are greatly on the increase, whereas fresh vegetables decline in favour of the ubiquitous tin as a labour-saving device.

Among the deficiencies, whether of dietetic or other nature, the discovery of which has so greatly influenced medical practice, the first to be explained was rickets. This was important not only in the practical results attained in children, but even more in showing the vital necessity of accessory food-factors, or vitamins. The triumph over rickets induced an endless stream of work on other vitamins and the bodily ailments associated with their deficiency, and this work is still in full swing.

Next came the evidence of a deficiency originating in the human body, and the explanation of the mechanism of Addisonian or pernicious anaemia. This work gave the urge to a re-investigation of many aspects of anaemia, to a complete re-classification of the diseases affecting the red blood-corpuscles, and to great improvements in therapy. We are probably just on the fringe of the discovery of other syndromes or diseases due to deficiencies arising within the body, and a pointer in this direction is the discovery of the effects of so-called vitamin K in the prevention of haemorrhage during obstructive jaundice.

Endocrinology

Advances in knowledge of the ductless glands and their secretions have been spectacular but have filled the medical world with major puzzles. Perhaps the most remarkable discovery of all has been the almost omnipotent importance of the small but doubly-constructed pituitary, and of the peculiar syndromes associated with disturbance of its numerous functions. The endocrine secretions and knowledge of their effects have progressed a long way since the discovery of adrenaline. In addition, however, to advancing practical knowledge, recent work on the endocrine glands has added to these puzzles. When insulin and its effects were made public in 1923, it looked as if the mechanism of one of the common diseases, diabetes mellitus, was finally solved. But it is now clear that this is far from the truth, and he

would be bold indeed who could venture to affirm today that he understands all the secrets of diabetes mellitus

Cardiovascular diseases

The limits of advance in knowledge of the mechanism of cardiac diseases with the help of the electrocardiograph seem to be approaching, and in practical medicine this instrument is far less used than formerly. There is still, however, a want of positive knowledge of the commonest cause of cardiac disease in youth, for the aetiology of rheumatic fever and chorea escapes us. Nor can much be said, except for the exclusion of syphilis as a cause, and its treatment when active, for the degenerative diseases of the heart and blood vessels. All new knowledge of syphilis and its active treatment has been fully utilized, and no doubt the bulk of syphilitic cardiovascular disease will gradually disappear. Reference should be made to one disease of this system which was long in becoming fully recognized but now takes such a prominent place in practical medicine. This is coronary thrombosis and coronary occlusion, which accounts for so many sudden disasters, even among members of the medical profession. High blood-pressure and its many complications still present unsolved problems both in aetiology and treatment, and the great contrast in prognosis in the two sexes still escapes us. Why should women often withstand high blood-pressure for so long, and men for so short a time?

Other trends which may be noticed in the study and treatment of cardiovascular disease are the increasing use of radiology, the diminished attention paid to cardiac murmurs, and the more careful assessment of symptoms as an indication of the state and reserves of the muscular pump as a whole.

Renal diseases

Here again questions involving the arterial system and the problems of pressor substances in the blood arise. Experimental work is at a promising stage, but so far nothing of practical importance in clinical medicine has emerged.

In spite of the comparative frequency of nephritis in civil life, and all the opportunity for work on acute glomerulo-nephritis which was provided by the epidemic outbreak in the last war, little information has accrued with direct bearings on any part of treatment, except in oedema. The use of the mercurial diuretics of the salyrgan group must be regarded as a major improvement both in cardiac cases and in the more chronic types of renal disease, and few, if any, other diuretics are now used in practice.

Gastro-intestinal diseases

The present state of our knowledge is unsatisfactory, although some of the common diseases are increasing. There is only one improvement to put against this, namely the decrease in constipation in women, coincident with the shedding of corsets and the increase in feminine athletics.

Everyone must be impressed with the great frequency of chronic gastric and duodenal ulcer, not only in men but also in women, and knowledge about aetiology remains as obscure as ever. Recently there have been considerable alterations in our methods of routine therapy, with a tendency to reduction in alkaline drugs and a more rational use of food, especially during bleeding. At present therapy, because of the poor knowledge of aetiology, must in the main be regarded as unsatisfactory in almost every respect. Interest in diseases of the small intestine is increasing in connexion with deficiency diseases, but there is no great progress to report.

The main developments in diseases of the colon centre round recognition

of the importance of psychological factors in aetiology and treatment. This is particularly true in connexion with our views on chronic ulcerative colitis; and some diseases purely psychological in their early stages at least, such as mucous colic, are on the decline.

Diseases of the respiratory system

Here the development of sulphonamide therapy, especially in inflammations, such as lobar pneumonia, is of the greatest importance, and the adequate and efficient use of oxygen, due to improvements in technique of administration, also calls for comment. Further, reference should be made to the use of the 'iron lung' in patients in whom respiration is hindered by paralysis of the respiratory muscles. There are many minor developments, but these are the most outstanding. The problems of pulmonary tuberculosis must also be mentioned, for much is being done in the recognition of early lesions by use of X-rays. Not only has it proved certain that X-rays are in early cases far superior to ordinary clinical methods, but this method has also been applied to the 'mass examination' of parts of the population at the age—fifteen to twenty-five—now recognised to be specially susceptible.

Diseases of the blood and blood-forming organs

The developments in knowledge of Addisonian anaemia gave the lead to a whole new series of investigations, and improvements can be recorded in all directions. The main classification of the anaemias has been altered, new and common disorders, such as idiopathic hypochromic anaemia, have been recognized, and treatment put on a much improved basis. Methods of investigation of bone-marrow function, such as sternal puncture, have added to knowledge, and the inadequacy of the older dosage of iron has been corrected.

Add to this the advancing technique and use of blood transfusion and of suitable substitutes for blood in haemorrhage and shock, and it is clear that, in this system and its diseases, great and valuable developments have occurred. The stimulus of war is likely to add even more to our efforts, for it was only during the last war that the recognition of 'blood groups' made blood transfusion practical and safe.

Few improvements, except the more efficient use of X-ray therapy, can be recorded in diseases affecting the white blood-corpuscles and the lymph glands and spleen.

The essential features of blood coagulation are still far from final solution, and the treatment of haemophilia, purpura, and other forms of the haemorrhagic diathesis is therefore imperfect.

Liver and biliary diseases

Little progress has recently been made. The use of vitamin K as a preventive of haemorrhage in obstructive jaundice promises to be a real therapeutic advance.

Nervous system

All the major advances seem to have come in association with endocrinology, and no improvements in knowledge or therapy have appeared in the common diseases such as disseminated sclerosis. The recognition of protruded intervertebral discs as the aetiological factor in a small percentage of cases of persistent sciatica must be mentioned.

Bone and joint diseases

These, if made for convenience to include the multiple forms of 'chronic rheumatism' and fibrositis, still represent a large uncharted sea in the world of Medicine, and the greatest cause of temporary industrial inefficiency or permanent human wastage. Taking as an example the problem of rheumatoid arthritis, the lack of knowledge of aetiology and successful treatment is pitiful. The explanation of focal sepsis is obviously inadequate and even the recent claims of gold therapy are far from being established. The value of local anaesthesia by novocain injection in fibrositis and kindred conditions must be regarded as a definite advance.

Psychology and psychiatry

Too much space would be necessary to refer to the influences, conscious or subconscious, of the work of Freud, Jung, and others on the problems of psychology and psychiatry, but they have obviously been great. The treatment of functional nervous disease is again assuming paramount importance in the circumstances of war, and it seems true that from every side the psychological aspects of disease, even organic disease, are receiving more and more recognition and attention from our profession.

Malignant disease

From the practical side there is little to report, except the steady spread of education among the public that malignant growths are at first entirely local, and that in the early stage many can be completely cured by surgery, X-rays, or radium. Moreover, it was proved long ago that cancer is not merely a disease of civilization, and that primitive races are not exempt. The trends and present state of development of cancer research are too little known, both to the public and to the profession, and demand a brief general summary.

There is first the forty-year old story of the knowledge of cancer in mice and its transmission by grafts to a variable proportion of other mice. This enabled many histological details of spread to be worked out under experimental conditions and yielded valuable information, some of it directly applicable to human disease. Then came the far-reaching discovery of the production of 'cancer at will', not simply in a proportion of experimental animals by grafts, but in every experimental animal by simple but repeated local applications of coal-tar to the skin. The cancer thus produced is typical in every way. Out of this work has naturally emerged a study of the carcinogenic properties of coal-tar derivatives, resulting in the important discovery that many of these resemble in their chemical constitution the sex hormones. What the final scope of this work may be is unforeseen, but it raises at once the problem of whether cancer begins from something intrinsic, produced within the body chemistry, or requires something beyond this to activate it. We think again of the older work of Peyton Rous and others, proving that one form of malignant disease in animals, a sarcoma, is due apparently to a filter-passing virus. No one who can view the work on cancer research as a whole can doubt that great progress has been made, even if so far this progress is not yet directly applicable to the cure of human malignant disease.

The future

What of the future? The attack on the problems of disease goes on, and must go on in spite of wars and other violent interruptions, as a part of human endeavour. Can the rapidity of progress in our generation be doubted by anyone? Progress cannot be continuous but is made in spurts, and often in quite unexpected ways. Gram is said to have discovered Gram's stain by accident while a medical student; yet his one day's work revolutionized

at the time the whole advancing study of bacteriology. Banting, on the other hand, by his discovery of insulin, set the last coping stone on a wall which had slowly been built up by many men before him. The slow building of these walls goes on—this work is known as 'medical research'—in the hope that some day the structure will be suddenly, and often quite unexpectedly, completed. The last stone falls into place generally so easily, as it appears after the event, that everyone is astonished by its apparent simplicity.

In the past the foundations of our clinical walls have too often been of crumbling stone and have quickly perished.

It seems fitting, therefore, to conclude this thumb-nail sketch of the position and trends of Medicine by calling attention to the work of Sir Thomas Lewis, who in recent years has preached the gospel of rebuilding our walls on the firm foundations of Clinical Science. His work brings us back to the fact that, in the march of medical progress, the human patient, with all his varying habits, reactions, and emotions, remains not only the source, but the final measure, of success.

GENERAL SURGERY

By G. GREY TURNER, F.R.C.S., F.R.A.C.S., F.A.C.S.
PROFESSOR OF SURGERY, UNIVERSITY OF LONDON, DIRECTOR OF DEPARTMENT OF
SURGERY, BRITISH POSTGRADUATE MEDICAL SCHOOL

SURGERY AND THE WAR

At the present time most surgeons are thinking in terms of the new situation which total warfare, with all its horrible realism, has thrust upon us. It is a truism that each conflict brings its own problems and that many are different from those that have occurred before. This is certainly so in the present struggle, for air-raid casualties with their multiplicity of injuries, the lesions caused by the 'blast' of high explosives, and wounds and burns produced by missiles at high temperature each introduce new experiences. In a way it is fortunate that we have been able to profit from the lessons learned in the unhappy conflict which overtook the Spanish people so recently. There it was proved beyond contention that in the treatment of war casualties the first intervention should be the main intervention and that, except for the treatment of urgent haemorrhage and elementary first-aid, there is little useful service to be fulfilled by the Aid Post and that all our organization should aim at getting the injured transferred to a fully equipped hospital as soon as practicable. This lesson took some time for its realization, but it does emphasize the great importance of the organization for the transport of the wounded in the chain of healing. Once the patients have arrived at a complete hospital it is desirable that they should remain under the observation of those surgeons who deal with the primary conditions until convalescence is well advanced. Unhappily in this as in other wars, the necessity for the provision of the maximum number of beds near the front line entails early evacuation and this interferes with the continuity of treatment and critical observation so essential for thorough evaluation of the methods employed.

In the treatment of fractured limbs the acceptance of the importance of absolute rest has developed the use of plaster of Paris and all surgeons who deal with the injured are realizing the extreme importance of the exact and accurate details of plaster technique. This 'plaster art' is difficult to teach in any way other than by actual demonstration. In open wounds of the soft tissues the most important part of the treatment is measures aimed at the anticipation of sepsis. The exploration of the wound and its mechanical cleansing by the removal of foreign bodies, ingrained particles, blood clots and so forth, and the excision of torn or otherwise damaged tissue are much more important than the use of antiseptics, irrigations, and the like. It seems to be proved that war wounds do best if free drainage is established from the first, and this can usually be best brought about by leaving the wounds entirely open. Though this appears to be somewhat of a revolution in surgical treatment, in contrast to the traditional wound suture, it is proving to be successful, and the present practice is merely to carry out the mechanical cleansing spoken of as 'wound revision' or 'débridement' and then to pack

the wound lightly with gauze, with or without vaseline, after which complete rest is provided by encasing almost the whole limb in plaster. It is rather a revelation to find, as recent military practice has proved, that in wounds limited to the soft parts, just as in fractures, the application of the principle of rest is of immense importance, and probably has just as much to do with repair as the form of dressing. In many cases the results have been surprising and wound healing has been much better than when closure by suture is added to the other procedures.

It may be impossible to ensure the sterility of the wounds by débridement alone, but an attempt is being made to bring this about in two ways: (i) by prophylaxis by drugs of the sulphonamide group by the mouth, and (ii) by the local use of the same drug. More time must elapse before it can be decided whether the condition of sterility brought about by these means or the absolute rest and complete drainage is really the more important. Experience which has so far accumulated about the use of chemotherapy in the treatment of head wounds goes to show that the circulating antiseptic is certainly of great value, for even when there has been no other primary surgical treatment than the application of a field dressing the wounds have done much better than experience teaches would have been the case if the drugs had not been employed.

True infective cerebritis and cerebral hernia both occur, but spontaneous recovery has often followed. In the presence of infection with gas-forming organisms gangrene has occurred, but not nearly so often as might have been anticipated. Whether this is the result of the prophylactic use of the sulphonamides or of gas-gangrene serum, or the combination of the two, is not yet settled and evidence is accumulating to show that free drainage and adequate rest are perhaps equally important. The success of the sulphonamides has prompted further investigation into the effect on the tissues of other chemical substances sufficiently powerful to have a bactericidal effect. As a result surgeons are gradually returning to the view that the value of antiseptics used locally is greater than the possible harm that they may do to the living tissues, but the search for the ideal antiseptic still continues.

With regard to the question of tetanus it has not been possible to estimate the effect of the sulphonamides as prophylactic agents because the great majority of those exposed to infection with the tetanus organism have been rendered immune, either actively or passively, by the prophylactic injection of toxoid or antitetanic serum. Active immunization by the toxoid has been employed for two years or more, and the evidence has proved it to be a most potent prophylactic agent. Nevertheless, unless there is an assurance that tetanus toxoid has been efficiently used there must be a resort to antitetanic serum, and for this purpose 3,000 international units is looked upon as the optimum initial dose, but when its administration is perforce delayed or in severe or heavily infected wounds 5,000 units may be employed. Thus far the prophylactic measures have been most successful for the incidence of tetanus has been only 0.45 per 1,000 wounded in contrast to the 8 per 1,000 in the early stages of the 1914-18 campaign.

The war has unexpectedly focussed attention on the question of burns, and although the tannic acid preparations have yielded such excellent results in civil practice, present experience rather suggests that some of the dyes may do even better. These dyes form a less dense and more pliable coating which is better adapted to the neck and face. Because of their antiseptic properties they may be widely used in association with the tannic acid, being painted or sprayed on the skin around the margins of the burnt area. The observation of large numbers of burns suggests that it is certainly a mistake to apply tannic acid to the fingers as its constricting effect interferes too much with the

blood supply and tends to necrosis or the development of fibrous tissue with much subsequent stiffening and disability. But it is not enough to treat only the burn; the general condition of the patient must claim a large share of attention. The treatment of shock, measures to combat fluid loss and plasma infusion may be essential. Fright and anxiety often play some part and the use of sedatives is of great importance.

There can be no doubt about the superiority of transfusions of whole blood in the treatment of haemorrhage, but in shock there is still much to be learned about the respective value of fresh blood, stored blood, and plasma, and for the moment it appears that plasma is more than holding its own in this race for superiority. Not only does plasma seem to be as effective as fresh or stored blood, but it seems to sustain the blood-pressure more effectively, and it has the supreme advantage that it can be given without blood grouping. But saline solution also has its place, and both experimental work and clinical experience are proving the value of a combination of hyper- and hypo-tonic solutions.

In the treatment of shock there is sometimes a tendency to forget the importance of ordinary measures such as rest, warmth, the relief of pain and thirst, and nourishment. As a result of the experiences of this present conflict there are already some who believe that these ordinary methods are probably as important as the intravenous injections. In the war of movement which has so far been the rule it has not yet been possible to deal with abdominal wounds as efficiently as in the last war, though fortunately there does not appear to have been any large proportion of these wounds. But all surgeons are prepared to be guided by the experience of the last conflict in the knowledge that in perforating lesions of the hollow viscera immediate intervention is likely to lead to the best results.

The controversy which has been revived about the guillotine amputation has raised doubts in the minds of onlookers, who are very properly asking if those who advocate this plan as entirely satisfactory and those who vehemently deprecate it, are not confusing the issue and are perhaps not discussing quite the same problem. Probably a compromise will evolve so that a simple circular amputation with nothing but short skin flaps will be recognized as the best method. The advantage of this plan may be further heightened by the knowledge that when infection is obviously gross at the time of intervention the wound can be left open. In these circumstances the flaps can be drawn together over gauze so that the difficulties due to skin retraction may be sufficiently minimized, and after healthy granulations have sprung up secondary suture is satisfactory. Even subjects such as the choice of the most suitable tourniquet, and the management of the avascular limb, have shown that there is much to ponder over in the most ordinary problems connected with surgery in warfare.

The fitness of men for the fighting services is a matter of the first importance and it is becoming recognized that the condition of the digestive and nervous systems and the way the recruit responds to a strange environment are no whit less important than the general physical development. Though we may be loth to admit it, there is a 'science of war', and the selection of those who are to take part, and their allocation to those duties for which they are best fitted is a most important function of the medical profession. Since we resolutely turned our faces against preparation for war we now find that we are lacking in what foresight might have provided. The protection of soldiers in the battle line from casualty is now also becoming more and more a practicable problem and it looks as if a return to armour, dull rather than shining, will become a necessary part of modern warfare as a prophylaxis against many body wounds. The bearing of the nutrition of the soldier on the healing of wounds is also of the first importance and especially since the very

rapid mobile warfare increases the difficulty of the bulky commissariat which is so essential to provide ordinary feeding. Supplementary rations in the form of tablets loaded with the necessary vitamins seems to be the ideal at which we must aim

REGIONAL SURGERY

Chemotherapy

Apart from warfare the applications of chemotherapy is proving extremely important in surgery. Its use is playing a part in the prevention of the complications of middle-ear disease and even meningitis seems to pale before its beneficial effect. Streptococcal septicaemia sometimes responds in a wonderful manner and more specialized infections, such as gonorrhoea, are also susceptible to modifications of the sulphonamide group of drugs. Up to the present pyelophlebitis has been a menace in all infections arising in the portal area and when it does occur it usually stalks on to an inevitable fatal conclusion, uninfluenced by treatment. Now there is some evidence that it also may yield to the sulphonamides, though more experience must be accumulated before we can speak with assurance in this connexion.

Diseases of the alimentary tract

To turn to more mundane matters it must be confessed that our hospitals still receive far too many cases suffering from the complications of appendicitis rather than from the initial disease. Every now and again we have to deplore the high mortality following the treatment of these complications, although it ought to be recognized that it has been proved again and again that, if only intervention can take place while the disease is still limited, recovery is almost as safe and sure as it is when the appendix is removed at an interval operation. In one series of nearly 600 cases the mortality of acute appendicitis limited to the appendix or its immediate vicinity was only just over two-thirds of one per cent compared with a mortality of just over one-third of one per cent for over 1,000 interval operations.

In rupture of peptic ulcer the insistence of the symptoms makes it less likely for the calamity to go unrecognized in the early stages, but it is not sufficiently realized that to attain a large proportion of successes it is necessary for these cases to reach the operating theatre within six hours of perforation. When that can eventuate the mortality is surprisingly low, and I can refer to a series of 58 duodenal perforations operated upon within six hours without a single death, and 247 gastric and duodenal ulcers treated by four operators, also within six hours, with a mortality of just over 4 per cent. It has been suggested that partial gastrectomy may still further improve the results, but this has not been borne out by such figures as are available, and on the face of it to substitute gastrectomy for simple closure of the perforation is going to place a very high tax on surgical accomplishment which must often be carried out by those who have yet to gain experience in the major surgery of the abdomen.

In the treatment of intestinal obstruction the decompression of the upper intestine by the use of the Wangenstein tube has undoubtedly helped to lower the still too high mortality, and there are hopes that the Miller-Abbott tube will still further help in this direction. But to rely on these measures alone may prove fallacious, for strangulations of all sorts will always require the earliest possible surgical intervention, always assuming that care is taken to make up for deprivation of fluids and salt before operating.

In the treatment of hernia the high road to radical cure is still not finally charted, and new expedients to that end are still advocated from time to time. The treatment by injection finds champions every here and there, but few now suggest that this method of treatment should supersede the radical cure in

healthy young adults. Probably it will remain as a stand-by for occasional use in those few cases in which there is some contra-indication to operation, and especially in old people, though there is no definite evidence that the injection method is entirely successful in the aged. Clearly a good deal more careful work checked by long continued observation after intervention is essential before any useful conclusion can be reached. It must, however, be admitted that the method has the outstanding advantage that it is ambulatory.

In the surgery of the biliary tract the question of operative injury to the ducts is every now and again being revived and of this condition it can be said with especial force that prophylaxis is infinitely superior to cure. If the accident is not recognized at the time of its infliction many of the patients die, and in those who survive, the intervention necessary for its repair is serious and attended with a high mortality. Among those who recover from this late intervention probably half suffer from the effects of persistent infection in the ducts or from recurrent calculi or from relapse as the result of stenosis of the repaired duct, and these conditions account for a not inconsiderable late mortality. There is only one certain way to avoid this surgical accident and that is for the operator to see the common bile-duct and the common hepatic duct before what is taken to be the cystic duct is caught and divided. When there is any possibility of error it is a wise plan for an assistant to examine the gall-bladder immediately after its removal in order to verify that the cystic duct alone has been divided. The preparation of jaundiced patients for operation continues to be recognized as of great importance, and much experimental work has been done with regard to the problems involved. The efficiency of vitamin K is being tested but all will agree that this in itself is not a panacea, but must be combined with the use of other plans of established reputation. The study of recurrent symptoms after apparently successful interventions for gall-stones and other biliary troubles has been assisted by cholangiography. There are a number of conditions that may account for failure of the primary operation in addition to recurrence of calculi, such as stenosis or persistent infection in the ducts. It is very curious how fashions in surgery alter, for the day is not long past when the Polya type of gastrectomy was almost universally accepted as the best. Now there is a tendency to go back to the old direct anastomosis of stomach to duodenum, which has been so long known as the Billroth I method. It has the virtue of being more or less a restoration of the parts and is physiologically sound, and it is therefore comforting to note that the after-results are probably better than by the other methods.

Varicose veins

In varicose veins everyone must admit that the treatment by injection has certainly fulfilled its promise, for the results are sometimes most remarkable. At the same time it cannot be expected that in all cases complete and lasting cure will follow, and it is a question of deciding how much benefit can legitimately be expected in those cases that are advanced, or in which the underlying aetiological factor cannot be dealt with. But the most important lesson which has become apparent is the recognition that there are many cases in which the maximum benefit can only be obtained by combining operative measures with injection therapy. This is especially called for when the vein in the thigh is extensively varicose. In some cases the best results follow the complete removal of the internal saphenous vein together with its posterior branch, but in others it suffices to divide and ligature this vein just below the saphenous opening while at the same time the lower portion of the vein is injected from its open end.

Congenital abnormalities

In these days, when the preservation of young life has become more than ever important, it is encouraging to note the increasing attention which is being paid to the management of those congenital anomalies which were formerly considered beyond relief by surgical means. Much can now be done for the victims of ectopia vesicae and it is known that the long-term after-results of transplantation of the ureter have been most encouraging, patients being alive and in good health 25 and 30 years after operation. The same principle of intervention is now being applied with more courage in congenital obstruction of the small intestine, in exomphalos, and in congenital obliteration of the bile-ducts. The problem of the congenital arrest of the development of the oesophagus is in a different category, but the ingenuity of surgeons is constantly being extended in efforts to supply means of relief, and there seems some prospect that such efforts may one day evolve a feasible plan.

Genito-urinary diseases

In genito-urinary surgery great attention is being paid to the aetiology of such conditions as hydronephrosis and enlarged prostate. Much work has been done on the treatment of enlargement of the prostate by hormones and, although this appears to be on right lines, at present the promise of effective treatment by this means is nebulous. In the operative management of gross enlargement resection by endoscopic methods is gradually finding its proper place, and the continued observation of large numbers of cases has proved that there is a considerable residue in which removal of the prostate by the older surgical plans is the best method of bringing lasting relief. In the management of stone attention to the underlying factors has intensified the belief that possibly some vitamin deficiency may have to do with the cause, and there seems some hope that it may be possible to control the diathesis. Such measures would confer untold benefit in those difficult cases of recurrent calculus formation which up to now have proved so resistant.

Undescended testis

The subject of imperfect migration of the testis also continues to sustain interest and the treatment by hormones seems to be gradually finding its proper level. But many who have particularly advocated this plan have evidently been unaware of the excellent results that follow operative interference by the method linked with the names of Keetley and Torek. This two-stage operation has now put surgical treatment on a very firm basis for good results can be predicted in the great majority of those cases in which it is properly carried out. There is now fairly general agreement that surgical intervention should not be undertaken until twelve years of age or later, but the operation is equally successful in older subjects. In many cases a testis in which development is retarded has undergone great improvement after its temporary residence in the thigh.

Cancer

In the operative management of cancer in general the treatment of the 'glands', better designated the 'lymph nodes', in the path of probable invasion is generally recognized as an essential part of the problem, and studies of later after-results certainly bear this out. Many surgeons are coming to recognize that, whenever practicable, surgical removal is better than all other methods, and there is much in the after-history of these cases to support that belief.

In cancer of the oesophagus new hope has been raised by the success of the operations for the removal of the thoracic oesophagus which have been

carried out and published by Garlock of New York, but the time which has elapsed since these efforts is too short to enable any report on their ultimate history. Simple non-malignant stenosis of the oesophagus is receiving more attention, and it may safely be stated that there are few cases in which this cannot be successfully managed by following the principle of dilatation, and there should be only a very small residue in which it is necessary to contemplate the formation of a new ante-thoracic oesophagus.

SUMMARY

In the attempt to assess the value of new procedures nothing is more important than continued observation over considerable periods of time—periods which must be measured in years, so far as most surgical problems are concerned. The enforced lull in ordinary surgical activity, for which the war is to blame, has almost called a halt in the surgical treatment of conditions like hypertension and cardiac ischaemia. But during this period of unparalleled anxiety careful observations of those cases which have already been operated upon will provide an admirable opportunity of assessing the value of the procedures which have been so enthusiastically employed during recent years.

OBSTETRICS AND GYNAECOLOGY

By JAMES YOUNG, D.S.O., M.D., F.R.C.S. ED., F.R.C.O.G.
PROFESSOR OF OBSTETRICS AND GYNAECOLOGY, UNIVERSITY OF LONDON, DIRECTOR
OF DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY, BRITISH
POSTGRADUATE MEDICAL SCHOOL

OBSTETRICS

Maternal nutrition—Haemorrhage in the new-born

Since the work of Rodda (1920) it has been known that the coagulation time of the blood exhibits a tendency to increase during the first five days of infant life and to return to normal within four or five days thereafter. Waddell and Guerry (1939) have shown that this period of increased coagulation time is associated with a reduction in prothrombin and this has been confirmed by Dam and his co-workers (1939), Nygaard (1939) and Quick and Grossman (1940). Nygaard and Dam have given evidence for the view that this transient hypoprothrombinaemia, when it exceeds normal limits, is sufficient to precipitate severe neonatal bleeding. The further discovery by Dam and his colleagues (1934, 1936) of the dependence of plasma prothrombin on vitamin K has opened up a new line of approach to the prevention and treatment of neonatal haemorrhage. Even under normal conditions the reserves of prothrombin or of vitamin K carried over by the infant from its prenatal existence are generally not sufficient to maintain the prothrombin level in the new-born until the time when vitamin K is absorbed in adequate quantities from the alimentary canal. When this inadequacy reaches serious proportions neonatal haemorrhage may occur. Macpherson, McCallum, and Haultain (1940) suggest that some morbid conditions in the mother (toxaemia, difficult labour) may specially lead to a serious drop in the maternal prothrombin and thus to a reduction in the prothrombin level of the new-born child. Macpherson, McCallum, and Haultain have addressed themselves specially to a consideration of intracranial haemorrhage in the new-born, which they believe may in many cases be caused by the slight trauma of labour operating in prothrombin-deficient infants. In this way they seek to explain the occurrence of intracranial bleeding when there is no adequate obstetrical cause. Further they believe that so long as the hypoprothrombinaemia persists the bleeding within the skull may continue and that therefore vitamin K may be of value even after a diagnosis of intracranial haemorrhage has been made. The authors summarize their views as follows. The administration of vitamin K or the synthetic active principle (a naphthoquinone), either to the mother between twelve and four hours before delivery, or to the new-born, would appear to be especially indicated (i) in cases of maternal toxaemia; (ii) in premature labour; (iii) in cases of instrumental or difficult delivery; (iv) when breast-feeding is not possible; (v) when any cerebral symptoms develop during the first few days of life; (vi) in cases of haemorrhagic diathesis, icterus gravis neonatorum, and anaemia; and (vii) when an operation is necessary on the new-born.

Permanent renal damage following eclampsia and pre-eclampsia

Dieckmann and Brown (1939) subject to careful critical analysis the evidence obtained both from their own clinic and from the published papers of other authors. They criticize the views of those, such as Herrick and Tillman and Peters, who ascribe hypertension, albuminuria, retinal changes or renal impairment discovered ten or more years after delivery to the effects of the damage produced by toxæmia during the corresponding pregnancy. They tend rather to support the view of Berman who raises the query 'does this perhaps point out that a great many cases of toxæmia really react to a constitution which has a defective cardiovascular renal system, that with such pregnancy and the added wear and tear of life, definite inroads on the durability of this system have been made; rather than that the toxæmia is the underlying cause of subsequent nephritis'. It is well known that a large proportion of women have persisting disability after a toxæmic pregnancy. Corwin and Herrick (1927) found persistent hypertension after eclampsia in 13 per cent, and after pre-eclampsia in 61 per cent of their cases. McKelvey and MacMahon in 1935 reported necropsy findings in 13 patients who died at varying periods after non-convulsive toxæmia. Although their clinical diagnosis had been chronic nephritis, in 10 the necropsy revealed a nephrosclerosis and not chronic glomerulo-nephritis. Dieckmann and Brown, after quoting these figures, stated that they had clinical records and necropsy sections from 21 eclamptic and 25 non-convulsive patients. There was no evidence of chronic glomerulo-nephritis in any of the eclamptic patients and only 5 of the non-convulsive group had this disease. Another patient died of acute nephritis. Those deaths not caused by uterine or other infection were due to cardiac failure, cerebral hæmorrhage or uræmia. They concluded that 'it is apparent from our own work and the reports of Corwin and Herrick, McKelvey and MacMahon, Peters, and others that chronic glomerulo-nephritis during or after pregnancy is a rare complication'.

Dieckmann and Brown refer to the significance of the 'toxæmic sequence' first described by Young in 1927. This author pointed out that in women with the toxæmic tendency in one pregnancy there was a greater risk of foetal disaster in other pregnancies in the shape of abortion, premature separation of the placenta, and still-birth. These conditions might or might not be accompanied by toxæmia. Thus the sum of these various conditions in 'normal' patients is 10·2 per cent, and in toxæmic patients is 23·2 per cent. The sequence in eclamptic cases is 44·7 per cent, and in pre-eclampsics 35·6 per cent. Dieckmann and Brown provide some confirmatory support to Young's findings. The authors' summary is as follows. *Eclampsia*. Subsequent pregnancies will be normal in 40 per cent of the cases and complicated by recurrence or exacerbation of the hypertension, oedema, or albuminuria in 40 per cent. Less than 10 per cent will have a recurrence of the eclampsia. Over 37 per cent of the patients had vascular renal disease, indicated usually by hypertension. No evidence of chronic glomerulo-nephritis was found in any of the eclamptic patients. *Non-convulsive toxæmia*. Subsequent pregnancies will be normal in at least 30, and probably 40, per cent of the cases, and complicated by a recurrence or exacerbation of the hypertension, oedema, or albuminuria in 50 to 70 per cent. More than 50 per cent of the patients had vascular renal disease, evidenced usually by a hypertension. Renal impairment, as indicated by a urea clearance of less than 50 per cent and due to nephrosclerosis, occurred in 2 per cent. Chronic glomerulo-nephritis was present in 0·5 per cent. They believe that true eclampsia and pre-eclampsia do not cause permanent vascular or renal damage and that when such damage occurs, either the condition was not eclampsia or pre-

eclampsia, or these diseases were superimposed on a patient with a pre-disposition to hypertensive arterial disease.

The investigations of Reid and Teel (1939) give results which are very similar to those of Dieckmann and Brown. The immediate prognosis was most favourable when eclampsia was uncomplicated with pre-existing vascular or renal disease and least favourable in cases with such pre-existing disease. In all cases followed up for an average of 7.6 years after eclampsia the incidence of a hypertension of 150 systolic or more was 27.5 per cent. In the group of patients known to have been normal prior to the eclampsia the incidence was 10.3 per cent, that is, the incidence of hypertension found in women of this age group irrespective of pregnancy. Further, in this group there was no instance of albuminuria or defective renal function. Reid and Teel did not find any evidence that simple eclampsia causes progressive glomerulo-nephritis and their impression was that eclampsia in the previously normal patient rarely indicates the chronic vascular degenerative process which results in progressive hypertension. The authors record similar findings in the follow-up of patients after an attack of pre-eclampsia.

Hormone factors in the toxæmias of pregnancy

Taylor and Scadron (1939) examined 21 cases of late pregnancy toxæmia and 17 cases of normal pregnancy and found a frequent but not invariable lowering of the blood and urinary figures for oestrogens and elevation of the prolactin values. A lowered pregnandiol excretion was also noted in a small series of toxæmia cases analysed. The tests for these hormones give only approximate values and the findings show wide variations between different individuals and even when different specimens from the same individual are contrasted. No hormone abnormalities were noted in 8 cases of unexplained bleeding and 2 cases of premature separation of the placenta. The authors observe that the hormonal changes in the toxæmic patients are perhaps associated with the cause of the toxæmia, but may simply be a secondary result of the disturbances of renal, hepatic, or placental physiology. Taylor and Scadron's work tends to confirm the observations published by Smith and Smith (1938), which should be consulted by those who are interested.

Retinal spasm in late pregnancy toxæmia

Mussey and Mundell (1939) state that examination of patients with severe eclampsia and pre-eclampsia generally demonstrates the presence of spasm in the small arteries of the retina, and of the capillaries of the nail-fold. Furthermore, in most instances, accurate retinal examination will show a difference between the retinal changes associated with vascular sclerosis or chronic nephritis and those found in acute late pregnancy toxæmia. They divide the retinal changes in the latter into four stages: (a) spastic narrowing of the arterioles, which may affect all branches of the central artery; (b) a stage in which irregular constriction of the lumen of the arterioles usually appears first or, to a more severe degree, in smaller nasal branches, and may vary from day to day; (c) a stage in which narrowing and constriction are more fixed and cotton-wool patches or haemorrhagic areas may appear; and (d) in which diffuse retinitis of the albuminuric type is found. They found that retinal changes were present in all cases in which the systolic blood-pressure was 200 mm. Hg or more, in 90 per cent of cases with a systolic blood-pressure between 170 and 200, and in only 52 per cent of cases with a blood-pressure of 160 or less.

Narcosis and foetal asphyxia

Henderson (1939) points out that all narcotics depress the respiratory centre of the foetus more than that of the mother. A considerable dose of morphine given shortly before delivery results in an apnoeic infant. This effect is even stronger with the barbiturates, and it is erroneous to believe that these drugs are preferable in this respect to morphine. Further, though the depressant effect of morphine can be largely countered by carbon dioxide, that of the barbiturates cannot be so controlled. Henderson urges that only narcotics with a relatively brief action are justified in labour and then only in the early stages. In the later stages, anaesthetics alone should be employed, for such drugs are of brief action and have relatively slight inhibitory effects on respiration. But even with anaesthetics precautions against asphyxia must be taken. Especially is this so in regard to nitrous oxide and the percentage of mixed oxygen should not be allowed to fall below 15 per cent. Otherwise asphyxial effects, immediate or delayed, similar to those of carbon monoxide asphyxia, may result.

Rosenfeld and Snyder (1939), who have done so much to elucidate the phenomenon of intra-uterine foetal respiration, have studied, as the result of direct visual examination of rabbit foetuses *in utero*, the effects of various narcotic drugs on foetal respiration. Following the intravenous administration to the mother rabbit of one or other of the non-volatile narcotics, pentobarbital sodium, paraldehyde, chloral hydrate, or morphine sulphate, they uniformly found that foetal respiratory movements were depressed or abolished at a level of dosage well below that required to narcotize the mother. Of the volatile anaesthetics ether, nitrous oxide, and cyclopropane were studied. During the administration of ether by the drop method foetal respiration became gradually depressed and ultimately ceased. Regular foetal respiration stopped well below the level of surgical anaesthesia in the mother. After stopping the ether, foetal respiration often reappeared as the mother animal recovered after elimination of the anaesthetic. With nitrous oxide the results were markedly influenced by the amount of oxygen available. When this was only present in a concentration of 10 per cent, foetal respiration was rapidly suppressed even before the mother showed much evidence of anaesthesia. With a mixture of nitrous oxide 85 per cent and oxygen 15 per cent, there was no depressant effect even after continuous administration for 40 minutes. With cyclopropane deep surgical anaesthesia of the mother could be reached and maintained without influencing foetal respiration. After delivery the foetuses survived without complication and did not show any of the striking signs of narcosis noted with the non-volatile drugs.

Leucorrhoea in pregnancy

Liston and Cruickshank (1940), in an examination of 200 pregnant women who were supposed to be suffering from leucorrhoea, found in 40 cases (20 per cent) normal vaginal contents with pus cells less numerous than epithelial cells, a flora consisting wholly of Doderlein's bacillus, a pH between 4 and 5, and glycogen abundantly present in the epithelial cells. Cervical lesions, including erosions, were present in 79 (nearly 40 per cent). More than half of these cases had other causes for the leucorrhoea. In 31, however, the cervix was the possible explanation of the leucorrhoea. The more severe forms of cervical lesion were associated with abnormal features of the vaginal contents; pus cells became more numerous, the bacterial flora contained Gram-positive or Gram-negative bacilli with or without Doderlein's bacillus, the hydrogen-ion value became higher and glycogen was less abundant in the epithelial cells. Gonorrhoea accounted for only 4 cases among the 200 women. The parasite of vaginal thrush was found to be the cause of the leucorrhoea in

49, or approximately 25 per cent. This infection was easily overlooked unless films were made from the white patches characteristic of the disease, when the hyphal filaments of the fungus could be seen. The blastospores of this fungus might be confused with yeast cells. *Trichomonas vaginalis* was by far the commonest cause of leucorrhoea in pregnant women. It was present in 75 (40 per cent). In all these cases pus cells preponderated over epithelial cells in the vaginal films, and in the majority of cases the flora consisted of a great variety and number of organisms, chiefly small Gram-positive and Gram-negative cocco-bacilli. The pH was generally between 5 and 6. In 8 cases it was impossible to determine the cause of the leucorrhoea.

GYNAECOLOGY

Stilboestrol

Schockaert and Ferin (1939, 1940) compare and contrast the physiological properties of the oestrogen stilboestrol and its esters obtained synthetically by Dodds and his co-workers with those of oestradiol and its benzoic ester. They give twenty-one physiological actions in which these substances correspond and four in which their respective biological properties differ: (i) stilboestrol inhibits, oestradiol stimulates, *in vitro* contractions of the uterine muscle induced by oxytocin, (ii) stilboestrol does not stimulate the thyroid when given by the intra-uterine route to castrated rats; (iii) it only induces feeble development of the mammary acini, (iv) applied locally it fails to inhibit the growth of the capon's comb as produced by testosterone or to diminish the surface-area of the cock's comb. With regard to toxicity they claim to show that the toxicity of stilboestrol administered parenterally slightly exceeds that of oestradiol, and that orally the toxicity of the former is distinctly greater. Stilboestrol may produce general malaise, nausea, vomiting, and anorexia, but in some reported cases they believe that the harmful results are due to the substance having been wrongly administered to patients with hyperhormonal menstrual troubles. Out of 30 patients with ovarian deficiency (amenorrhoea, castration, or natural menopause) 6 showed an early and 15 a late intolerance. Among 44 parturient women one only—a uraemic patient—was intolerant. They conclude that stilboestrol or its esters administered by the intramuscular route in doses of 0.05 mg. (diacetate) or of 0.75 mg. (dipropionate) with a maximum daily dose of 2.5 mg. are unlikely, in the great majority of cases, to cause toxic symptoms. After labour or abortion oral dosage with stilboestrol may with advantage replace oestradiol to suppress mammary activity. Stilboestrol deserves trial in conditions of ovarian deficiency, but the dose should not exceed 0.5 to 1.0 mg. daily, and great care must be taken in conditions requiring large doses, such as 5 to 10 mg. daily. In another communication, Schockaert and Ferin (1940) refer to the value of stilboestrol in cases of vulval atrophy, menopausal symptoms, amenorrhoea, and other conditions. It is at least twice as active as oestradiol and oestrone when given orally. Lactation was inhibited in 15 out of 36 cases. Toxicity varies with the clinical conditions for which the drug is used, thus in cases of ovarian deficiency the authors found that 50 per cent of the patients were intolerant, whereas in the puerperium most women tolerate it well.

Testosterone propionate in functional uterine bleeding

There is now a considerable recent literature on this subject which tends to show that used with caution the male hormone may be classed amongst the active conservative methods for the treatment of excessive and irregular uterine bleeding of 'functional' origin. Mazer and Mazer (1939) treated 38 women. In 29 there had been metrorrhagia for periods averaging 12 weeks,

in 9 of these there had been menorrhagia for periods averaging 17 months. Testosterone propionate in sesame oil was given intramuscularly thrice weekly for 2 to 9 weeks, the individual dose varying between 2.5 and 25 mg. In a follow-up ranging up to 19 months and averaging 8 months, 26 out of the 38 women were cured and 12 were only temporarily or not at all relieved. In 30 women, in whom the menstrual rhythm had been previously regular, this rhythm was not changed. There was no obvious reduction in fertility and 4 patients conceived within 1 to 10 months after the suspension of the treatment. Most papers warn against the risk of virilizing effects which, especially when large doses are used, may cause much discomfort and distress. There are hirsuties and lowering of the pitch of the voice, enlargement of the clitoris, increase in weight, and there may be, in addition, an acneiform eruption on the face. Patients should always be warned against these risks before the treatment is commenced.

Effect of oestrin on breast tissues

It is well known that oestrogens, especially when given in massive doses, may provoke overgrowth of the mammary tissues and in some cases this may result in marked symptoms due to swelling and tenderness. Because of the suspicion that the massive dosage of oestrogens often employed clinically may sometimes possess carcinogenic properties some gynaecologists have from the beginning been timid in their use. Although in some animal experiments oestrogens have apparently been shown to be carcinogenic there is, however, no reliable evidence of such an influence in the clinical field. Hoffmann (1939) observed the influence of large doses of oestrogens on the structure of the breast in women, the biopsy material being obtained during the performance of plastic operations. In one woman past the menopause, who had been given 50,000 international benzoate units, he found marked hyperaemia and an increase in the milk ducts. In a second woman of the menstrual age, who had been given 250,000 units, the breast showed marked hyperaemia and an increase both of the acinar and duct tissue. Allaben and Owen (1939) record a case in which adenocarcinoma of the breast developed in a woman nearing the menopause who received 250,000 units of oestrin over a period of one year. The authors do not claim that the neoplasm was necessarily induced by the drug but they record the case as a possible warning. It is clear that the only way in which such a potential carcinogenic risk can be adequately assessed is the accumulation of increasing evidence and that, until this is available, clinicians must be cautious in the employment of oestrogenic agents especially in women advanced in years and when long-continued treatment is contemplated.

Pregnanediol

Cope (1940), employing the Venning method for extraction, has carried out an extensive quantitative assay of pregnanediol excretion in the urine in normal women and in selected clinical conditions generally regarded as implying ovarian hypofunction. His observations confirm the claims of Venning and Browne (1937) that pregnanediol is excreted in the urine only during corpus luteum activity. He has confirmed in several women examined that pregnanediol is excreted during the luteal phase of the menstrual cycle, that it falls to zero before bleeding commences, and that it is absent from the urine during the first or pre-ovulatory half of the cycle. In contrast to this it was shown that no such excretion occurred during a period of several weeks in two women suffering from secondary amenorrhoea. A woman was studied who suffered from excessive uterine bleeding in whom a clinical diagnosis of non-ovulatory bleeding had been made. The fact that no

trace of pregnanediol was excreted during a time which included three uterine bleedings provided additional evidence of the close association between corpus luteum activity and pregnanediol excretion. Cope was able to confirm that pregnanediol could be made to appear in the urine after injection of progesterone, but the recovery of the substance had in all cases been small. Until more definite evidence to the contrary has been produced, it must be assumed that the observed pregnanediol excretion represented only a small proportion of the total endogenous progesterone production

The pH of the vagina and cervix

Pierra (1939) tested the pH of the vagina in 261 women. In 216 cases the figures ranged between 4.5 and 5.2 with an average of 4.6 which was regarded as normal. In 42 cases (16 per cent) the readings were high, the highest being 6.8, whilst there were only 3 cases with figures less than 4.5. Lactic acid formation and the activity of the Döderlein's bacillus stopped below this level. The pH of the cervix was investigated in 259 cases. In 162 the readings ranged between 6.0 and 7.6, with an average of 6.8, which was regarded as normal. 84 women (33 per cent) had a reading less than 6.0, whilst 13 (5 per cent) had a reading greater than 7.6. The pH of vagina and cervix varied throughout the menstrual cycle. In 20 per cent the vagina was less acid in the mid-cycle phase, whilst the cervical pH rose about the time of ovulation and was lowest just before and after menstruation.

Cervicitis and cervical erosion

Wollner (1939) states that the histological interpretation of endocervicitis and erosion and the deductions therefrom are based upon the assumption that the cervical mucosa maintains a constant histological structure and fails to recognize the cyclic changes due to ovarian hormonal activity. In previous papers he had demonstrated menstrual cyclical changes in the cervical mucosa and he believes that these various phases of the endocervix have been erroneously interpreted as denoting inflammation just as some of the cyclic phenomena of the endometrium had been designated chronic glandular endometritis before the discoveries of Hitschman and Adler early in the century. To demonstrate the influence of the ovarian hormones on the cervix he carried out experimental studies in 6 women in whom ovarian activity had been arrested at the menopause or after castration. He found that progynon B (oestradiol) caused stimulation of the gland elements with hyperaemia and oedema of the stroma and that large doses changed the atrophic mucosa with the production of active glandular hyperplasia, and the appearances found in the characteristic picture of 'endocervicitis'. Proluton injections tended to stimulate the squamous epithelium and to inhibit the influence of the oestrogen. He believes that a considerable number of cases of so-called chronic cervicitis and erosion are merely the result of changes in the cervix produced by varying or morbid activity of the ovarian hormones.

Bourne and Bond (1940), in a discussion of the pathology of cervicitis, suggest that hormonal influences, possibly over-production of oestrin, are a factor, if not the paramount factor, in the causation of many cases of so-called chronic cervicitis, and that genuine bacterial infection is by no means always present in cases of excessive cervical discharge. They were impressed by the comparative absence of the true signs of inflammation in a very large number of cervixes amputated for leucorrhoea. In many cases these exhibited very advanced macroscopic signs of what is commonly called 'cervicitis', usually ascribed to the effects of chronic inflammation. The symptom regarded as typical of cervical inflammation was leucorrhoea, while the signs were erosion, enlargement, eversion, and follicles. It was obvious that there were a number

of cases of true cervicitis, as for example those of gonorrhoea and an occasional pyogenic infection following labour or abortion but, if these were excluded, the majority were found to show very little beyond hypertrophy of all the tissue elements and increased activity of the gland cells. Many erosions even showed only the slightest and most superficial inflammatory reaction, such as might be caused by contact of columnar epithelium with the acid medium of the vagina. Bacteriological examination of the cervical canal and mucus expressed from the deep glands and follicles also showed little evidence of active infection, always excepting gonorrhoea. In transverse sections of the cervix there might be enormous hypertrophy of the gland layer without any sign whatever of inflammation, whilst in longitudinal sections the gland layer was seen to extend on to the portio, where there was an erosion in which the superficial layers, only, showed some chronic inflammation which ceased abruptly at the external os.

Needle puncture of posterior fornix

Schultz (1939) states that between 1919 and 1938 puncture of the posterior cul-de-sac from the vagina confirmed the diagnosis of tubal pregnancy in 345 cases at the University of Hamburg Gynaecological Clinic, and that in 14 cases the puncture gave erroneous evidence. The aspiration of blood is definite proof of ectopic pregnancy if blood in the peritoneal cavity derived from endometriosis or ruptured ovarian cyst be excluded. Puncture was also employed for the determination of the nature of a pelvic swelling when this was obscure. The material obtained was fixed in alcohol, sectioned and submitted to the microscope. In 45 out of 54 such masses a correct diagnosis was possible. Puncture was also employed in subacute and chronic cases of pelvic inflammation; it should be avoided in acute cases. The procedure is useful for diagnosis, and aspiration of the fluid contents of inflammatory masses is of great therapeutic value in promoting absorption. Schultz followed up 301 such cases for at least five years. In 218 complete cure resulted, in 36 a second course of conservative therapy was necessary, and only in 47 was a subsequent more radical operation necessary. In 47 (15 per cent) pregnancy followed and 31 of these went to term. In discussing the dangers of puncture the author states that in 20 or 30 out of 2,000 cases the bowel was punctured without harmful results. Bleeding may occur, especially if the puncture is not mesial; it is rarely severe and can generally be controlled by suture or a vaginal pack. Intra-abdominal bleeding never occurred.

Tubal sterilization

Von Graff (1939) has collated 4,279 cases of artificial sterilization by the Madlener method (ligating a loop of tube on each side) showing an incidence of success in 99·7 per cent. The author records 304 personal cases with one failure. The causes of failure are stated to be mistaken ligation of the round ligaments instead of the tubes, slipping of the ligatures and lacerations of the peritoneal surface of the tubes, which predispose to fistula formation. The author believes, also, that cutting of the ligated loop of the tube predisposes to failure.

Reopening of tubes sterilized by ligation.—Rubin (1938) showed that when fertility is desired after tubal ligation it may sometimes be possible to re-establish the lumen by uterine insufflation with carbon dioxide. In 5 such patients patency was established by pressures below 160 mm. Hg. The more recent the ligation the less pressure is required and for this reason it is unwise to practise insufflation as a test of success soon after a sterilizing operation has been performed. Unless the interstitial position of the tube

has been resected the artificially induced obstruction should yield to an insufflation pressure of 200 mm. Hg or less. In experienced hands the pressure may be increased to 250 mm. An attempt which fails at first may succeed at a later date

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ALIMENTARY TRACT DISEASES

BY SIR ARTHUR HURST, D.M., F.R.C.P.
CONSULTING PHYSICIAN, GUY'S HOSPITAL, LONDON

DIGESTIVE DISORDERS IN SOLDIERS

In the war of 1914-1918 gastric disorders were comparatively rare among soldiers. In contrast with this, in the present war a large proportion of men sent home from France were suffering from digestive disorders. In some of the early convoys the proportion was as high as 40 per cent, and the total up to the emergency evacuation of base hospitals in April, 1940, was 14.4 per cent. At the request of the Royal College of Physicians of London, Charles Newman and Reginald Payne carried out an investigation into the nature, cause, and possible prevention of such disorders. They examined all of 196 cases of the kind in six Emergency Medical Services hospitals, as well as 89 similar cases among men who had not served overseas and who had been admitted into the military hospitals at Netley and Aldershot. The following table summarizes the diagnoses made in these two series of cases.

Analysis of 285 Cases of Digestive Disorders in Soldiers

	CASES FROM FRANCE	CASES FROM ENGLAND	TOTAL
Proved ulcers	165	59	224
duodenal	123	41	164
gastric	25	16	41
uncertain	7		7
gastric and duodenal	5	2	7
anastomotic	5		5
Presumptive ulcers	13	9	22
Carcinoma	0	1	1
Gastritis and duodenitis	5	2	7
Functional and indeterminate			
dyspepsia	9	6	15
Non-gastric diagnosis	4	12	16
Total	196	89	285

Many minor cases of dyspepsia were kept in France, the large majority of those sent home having been diagnosed as suffering from definite organic disease after thorough investigation. In spite of this the two series were very similar.

The table shows that nearly all the cases were organic, ulcer being the one common disease. Duodenal ulcer was four times as common as gastric ulcer. No less than 92 per cent of the men had suffered from ulcer before they joined the Army. Most of them were reservists, who should never have been allowed to rejoin. Questions about previous dyspepsia had rarely been asked by medical boards. Many men did not like to complain of indigestion, and others did not mention it as they were free from symptoms when examined. In a few a gross error was made by the Board in passing

them for service when they were pale or wasted or had abdominal scars. Several had undergone an operation for perforation of an ulcer (P. H. Willcox). Willcox obtained a family history of ulcer in 35 per cent, and of dyspepsia in an additional 10 per cent of 40 soldiers with ulcer evacuated from France in contrast with 4 per cent and 2 per cent respectively among 50 soldiers with no digestive disorders. I have frequently drawn attention since 1921 to the familial character of the ulcer diathesis (Hurst, 1921).

The cause of the recurrence of ulceration appeared to have been the change from the comparatively strict diet which nearly all had followed for years in civil life to the heavy Army food. The quality of this was on the whole good, but the cooking was almost invariably bad. There was much complaint about its greasiness, and the meat ration was excessive. Many men replaced their rations by food bought outside and so kept fit whilst they were still in England, but in France this became impossible and a breakdown followed. There was a considerable deficiency in vitamin C in the diet, fresh green vegetables being rarely provided and fruit never, but it is not likely that this helped in the development of the ulcer. The teeth were inadequate for chewing in 38 per cent of the ulcer cases - an important factor in view of the heavy food and large meat ration. In only 13 per cent was there much dental sepsis. Excessive smoking was probably a frequent accessory cause (Willcox). Psychological factors appear to have been of little, if any, importance.

The age at the onset of ulcer symptoms was surprisingly low - in 40 per cent it was under 25. Vomiting was a much commoner symptom of duodenal ulcer than in civil life, probably owing to the unsuitable diet. It was often the determining factor in making a man go sick.

As the higher age groups are conscripted for military service, the proportion of men suffering from ulcer is likely to increase, unless more care is taken by medical boards to reject all men suffering from ulcer and all who can bring clear evidence of having had an ulcer, however long they have been free from symptoms.

SURGICAL TREATMENT OF ULCERATIVE COLITIS

Before discussion of the question of the surgical treatment of ulcerative colitis it is necessary to recall how successful medical treatment is in the large majority of cases if carried out with sufficient care and patience. This is well seen in the following statistics of patients with ulcerative colitis who received some form of treatment whilst at Ruthin Castle (Spriggs) or in New Lodge Clinic (Hurst) from 20 years to 1 year prior to 1937 (Hurst, 1935).

	RUTHIN CASTLE	NEW LODGE CLINIC	TOTAL	PERCENTAGE
Quite well	34	32	66	77.6
Not well, but improved and 'keeping about'	5	4	9	10.6
Ill	1	1	2	2.4
Dead	5	3	8	9.4
Total	45	40	85	100

A discussion on the surgical treatment of ulcerative colitis held by the Section of Proctology of the Royal Society of Medicine on May 8th, 1940, showed that appendicostomy or caecostomy is still the favourite operation of most surgeons. Ogilvie and Corbett, however, advocated ileostomy, and

I have no doubt that this operation is more rational and gives much better results.

Before the last war and again in 1920 I had an appendicostomy performed on several of my cases of ulcerative colitis. But I gradually came to the conclusion that the operation was of little or no value. It can be shown with X-rays that the caecum can always be reached by running a pint and a half of fluid *per anum* and that the colon, especially when it is abnormally irritable as in ulcerative colitis, is completely evacuated by this means. There is consequently not any advantage in the injection of the fluid from above. A considerable number of the worst cases I have seen, many of which were subsequently cured by prolonged medical treatment, had already had an appendicostomy performed, but the opening had been allowed to close when improvement had not followed. The majority of the cases included in the statistics quoted at the meeting of the Proctological Section would doubtless have got well just as quickly without operation with the medical treatment which they all received at the same time.

When ileostomy is performed each case must be judged on its merits before deciding whether the opening should be permanent, or whether later the divided ileum should be rejoined or colectomy followed by ileo-sigmoidoscopy should be performed.* There are three indications for ileostomy. (i) The only hope for the very rare acute fulminating cases with high temperature and passage of large quantities of pus and blood is ileostomy. Courage is required to operate on such a case, but I have seen an amazing improvement occur within twenty-four hours with ultimate complete recovery, the divided ileum being rejoined some weeks later without any recurrence. (ii) When continuous medical treatment under good conditions for about nine months has not led to any real improvement. (iii) Very chronic cases which have already developed fibrous strictures or true or pseudo-polyposis by the time they come under observation.

Very few cases have given any trouble after ileostomy. I have rarely seen the severe diarrhoea and dehydration often mentioned as sequels. This is because I always examine the patient after an opaque meal to see if there is undue hurry through the small intestine. When this occurs the associated enteritis must be controlled before performing ileostomy. Any looseness which develops later can be controlled by diet and codeine. It is remarkable how comfortable patients are with an ileostomy. They can lead a life of normal activity, and with a well-made apparatus the ileostomy gives no more trouble than a successful colostomy. Two of my patients were girls of about 20, who were able to play lawn tennis, dance, and enjoy life for a couple of years before the stoma was closed, and others were professional business men who are quite reconciled to a permanent ileostomy. One man writes that in the two years which have elapsed since the ileostomy was performed he has led a normal life and has been continuously at work as an analytical chemist. He works in his garden and can walk ten miles in a day without ill-effect. Another, who had a colectomy performed in addition to a permanent ileostomy on account of continuous discharge of blood and pus *per anum* caused by numerous secondary polypi, four years later is leading a normal life and enjoys walking, dancing, and skating.

Though Ogilvie recommends closure of the distal end of the divided ileum, I think it is preferable to bring both ends to the surface some distance apart. When no more blood or pus is passed *per anum* the colon is washed out with water from above and the deposit is examined microscopically. If no red corpuscles or pus cells are present and endoscopy shows a healthy mucous

* The majority of my patients have been operated upon by Mr. Gaymer Jones of Windsor and most of the remainder by my surgical colleagues at Guy's Hospital.

membrane, the colitis can be regarded as healed. An X-ray examination of the excluded colon generally shows that the empty colon is much contracted with complete absence of haustration; but this might occur if it were healthy, as haustration is the manifestation of the activity of the muscularis mucosae, the function of which is to mix the colonic contents.

Before a second operation is undertaken an attempt should be made to increase the resistance of the bowel wall by the injection for several weeks of some of the faeces discharged from the ileum through the distal ileostomy opening. The faeces are first diluted with water and gradually made stronger, till finally the whole of the ileal contents are injected undiluted. If there is no reaction it is probably safe to rejoin the divided ileum. But the mucous membrane may have been replaced over large areas by a single layer of flattened epithelial cells, the resistance of which must be very much less than that of a normal mucous membrane. If therefore the disease is of very long standing so that it appears probable that much of the mucous membrane has been replaced by a simple epithelial lining, or if strictures or polypi are known to be present, it is safer to perform colectomy. This should also always be undertaken if a year after performance of the ileostomy blood and pus are still being excreted *per anum*. The colon should be excised down to a point about nine inches from the anus. It is then generally possible by local treatment from below, including diathermy cautery for polyps and for dilatation of strictures with a rubber bag, to restore the remaining colon sufficiently for the ileum to be joined to it after another interval of several months. If, however, this should not occur, the remaining part of the pelvic colon and rectum can be excised and the patient must become reconciled to a permanent ileostomy.

I regard surgery on the individualized lines described above as the most important advance in the treatment of ulcerative colitis in the last ten years.

HEPATITIS

Aspiration biopsy of the liver

Roholm and Iversen (1939, a) of Copenhagen devised a safe method of performing aspiration biopsy on the liver. A column of hepatic tissue measuring 1 to 2 cm. in length and 2 mm. in diameter, which is sufficient for a satisfactory histological examination, is obtained. By this method, which they have performed in over 200 cases, they were able to demonstrate the presence of acute and chronic inflammatory and degenerative lesions, cirrhosis, primary carcinoma, fatty and amyloid degeneration, the deposition of iron in haemolytic jaundice and haemochromatosis, and leukaemic infiltration. It is likely to prove a method of considerable value when difficulty is experienced in deciding whether jaundice is hepatic or obstructive in origin; in the latter large casts or accumulations of bile are found between the unchanged parenchymatous cells.

Catarrhal jaundice and acute hepatitis

The most important results so far obtained by means of aspiration biopsy of the liver is in connexion with the difficult subject of catarrhal jaundice. Roholm and Iversen (1939) performed 38 biopsies in 26 sporadic cases of so-called catarrhal jaundice. The jaundice generally appeared a few days after the onset of illness, gastro-intestinal symptoms had been present in 18 of the 26 cases. The duration of the jaundice varied between 3 and 12 weeks; the biopsy was generally performed about a week after the appearance

of the jaundice and sometimes again a month later when the patient was convalescent.

In every case a diffuse hepatitis was found. This was characterized by (i) inflammatory changes in the connective tissue with a majority of mono-nuclear cells; (ii) destruction of the trabecular structure of the liver and necrotic disintegration of the parenchyma cells, especially in irregular foci of variable size; and (iii) proliferation of connective tissue in the portal spaces and diffusely in the lobuli. Unexpectedly, the liver cells contained a normal amount of glycogen (Krærup). The interlobular bile-ducts were normal and there was not any change in the Kupffer cells. The hepatitis was fully developed a week after the onset of jaundice and had generally subsided within a month of disappearance of the jaundice. All evidence of disease may eventually disappear and the normal trabecular structure be completely restored. In other cases slight or moderate increase in connective tissue persists.

In one case, which began as ordinary 'catarrhal jaundice', severe symptoms appeared on the twelfth day and the patient died in coma on the fifteenth day. Biopsy performed 16 hours before death showed the usual parenchymatous destruction and the connective-tissue inflammation characteristic of acute hepatitis, but much more severe. Ten hours after death tissue obtained in the same way showed advanced necrosis of the parenchyma, which failed to stain, in striking contrast with the specimen obtained in life 26 hours earlier, the parenchyma of which stained well. The histological changes in other cases of acute necrosis were similar, and Iversen and Roholm conclude that the complete necrosis observed in acute atrophy of the liver (acute hepatic necrosis) is a post-mortem phenomenon.

The jaundice is presumably in part a result of impaired functional activity of the parenchymatous cells, which normally take up the bile pigment from the Kupffer cells and excrete it into the bile canaliculi. The cells often contain bile-pigment granules, which are never seen under normal conditions. Disorganization of the trabecular structures with the resulting dissociation of the liver cells must also interfere with the excretion of bile by causing rupture of the bile capillaries.

Thune Andersen, from his study of the disease in Denmark, concluded that it is caused by an infection of the alimentary canal, probably with a virus. Thus in the majority of cases the jaundice is preceded by gastro-intestinal symptoms and its incidence, like that of dysentery, is 8 times more common in country districts in Denmark than in Copenhagen, in striking contrast with diphtheria, which is spread by droplet infection and is more common in the city, and scarlet fever, which is spread in both ways and has an intermediate distribution. It is possible that in Denmark the infection is conveyed by the consumption of pork, as a form of hepatitis similar to that in man occurs in pigs. Andersen succeeded in transferring the disease to healthy pigs by feeding them on the liver of jaundiced pigs, and he also produced acute hepatitis in pigs by feeding them with bile obtained through a duodenal tube from patients with acute hepatitis.

The high incidence of acute hepatitis in Denmark compared with Great Britain may be due to the fact that pork is the main animal food in Denmark and that it is often eaten uncooked or partially cooked as paste and in sausages. E. G. White, of the Royal Veterinary College Research Institute, tells me that jaundice does not occur in pigs in England, though a virus could remain alive in imported bacon. The virus of swine fever has in fact been found in bacon, generally in the bone marrow, and it is regarded as a possible source of infection of pigs in England. Possibly, too, some of the liver paste and liver sausage sold in 'delicatessen' shops may be imported. If Andersen's

views as to the origin of the infection in acute hepatitis are proved to be correct, it will, I think, be found that the disease is rare in England and that most cases of 'catarrhal jaundice' here are caused by catarrhal obstruction of the common bile-duct and are not primarily hepatic. Evidence for the existence of a true catarrhal jaundice was brought forward in a paper I wrote with Simpson in 1934. Definite proof of its existence, though very rarely obtainable owing to the absence of post-mortem material, was afforded by Eppinger's case, quoted in our paper, of a girl of 19 who committed suicide at the height of an attack, and in whom the mouth of the dilated common bile-duct was narrowed by inflammation of its wall and completely obstructed by a plug of epithelial detritus and pus, and no trace of disease was discovered on microscopical examination of the liver

It is to be hoped that aspiration biopsy of the liver will be systematically performed in sporadic and epidemic cases of infective jaundice in England, as it is only by this means that the relative frequency of true catarrhal jaundice and acute hepatitis will be ascertained.

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DISEASES OF THE BLOOD-FORMING ORGANS

By J. E. H. WHITBY, C.V.O., M.C., M.D., F.R.C.P.
ASSISTANT PATHOLOGIST, THE BLAND-SUTTON INSTITUTE OF
PATHOLOGY, MIDDLESEX HOSPITAL, LONDON

HAEMORRHAGIC STATES

In 1934 Dam discovered vitamin K and in 1938 Dam and Glavind began to link up this fat-soluble vitamin with the deficiency of plasma prothrombin found in severe liver disorders, especially those associated with jaundice. Since 1938 the application of this work to the treatment of many haemorrhagic states has rapidly become important. Prothrombin is essential for efficient coagulation of the blood, and it is now known that vitamin K is used by a healthy liver in the synthesis of prothrombin. Hence either or both of two conditions may result in plasma-prothrombin-deficiency, namely failure to absorb the vitamin and disease of the liver sufficient to prevent prothrombin synthesis. Because vitamin K is fat-soluble any derangement of the digestion of fat tends to interfere with its absorption. This is the reason why the vitamin, administered with bile in order to ensure absorption, has been found to be so useful in the prevention of the operative and post-operative haemorrhages frequent in surgical jaundice and in a number of conditions in which metabolism of fat is disordered. It has, however, been found that the hypo-prothrombinaemia associated with parenchymatous hepatic disease does not respond to treatment in the same way as when the deficiency is due to lack of absorption (Kark and Souter). Synthetic compounds, allied to and as effective as the natural vitamin, can be prepared. Of these synthetic compounds, 2-methyl-1,4-naphthoquinone is an example: this and other similar substances are as potent as the alfalfa and fish-meal compounds which are rich but unpalatable natural sources.

The most interesting and enthusiastic developments of this theme have been its application to haemorrhagic disease of the new-born and an attempt to extend its utility to include the haemolytic neonatal anaemias and allied conditions. Research has shown that the prothrombin level in infants is normal at birth, drops abruptly during the first few days of life, and then rapidly becomes normal (Quick and Grossman). These early deficiencies are even more pronounced in premature infants (Hellman and Shettles). In an adult, vitamin K is absorbed in the intestine directly from food in the presence of bile, and from the colon, where vitamin K may be synthesized by bacterial action. In an infant, however, milk is a poor source of vitamin K, and the contents of the intestine are sterile. Hence it is assumed that only small amounts of vitamin K can be absorbed until bacterial invasion of the bowel occurs. These are suggested as the reasons why the prothrombin level during the first few days of life may be dangerously low. Abnormal bleeding in the new-born appears to coincide with prothrombin deficiency, and neonatal haemorrhage can be favourably influenced by administration of vitamin K (natural or synthetic) either to the infant after birth or to the mother 12 to 24 hours before delivery (Macpherson, McCallum, and Haultain). For haemorrhagic disease of the new-born presenting itself as melaena or haematemesis vitamin K therapy is undoubtedly rational, but it is as well to be critical of the suggestion that such treatment may also be of value in other neonatal diseases and conditions.

It has been recommended that vitamin K should be given to all infants born under conditions which tend to reduce prothrombin. Such conditions include maternal toxæmia, premature labour, difficult labour, and whenever breast feeding is not possible. This last because breast feeding supplies small quantities of harmless bacteria which assist in establishing an intestinal flora. It is well known that a blood clot is not firm unless the plasma prothrombin is adequate. It is therefore claimed that, when there have been signs of intracranial hæmorrhage during birth, vitamin K may well help to avoid later cerebral hæmorrhage (at a time when the prothrombin level is at its lowest) due to secondary oozing from a soft clot loosened perhaps by restlessness or by a sudden cry (Macpherson, McCallum, and Haultain). For the same reason it is a wise precaution to administer vitamin K whenever operations have to be performed on the new-born. In all of these conditions there is a sound theoretical reason for the treatment, but the same cannot be said for vitamin K therapy in icterus gravis and other neonatal anaemias. It is necessary carefully to distinguish the jaundice of icterus gravis from the hæmorrhagic tendency which is associated with the disease because of the jaundice, it is the hæmorrhagic tendency which vitamin K influences and not the primary disease itself. Finally it should be borne in mind that vitamin K is useless as a non-specific hæmostatic and is therefore without any value in hæmophilia, purpura, or intrinsic diseases of the blood-forming organs.

ALEUKAEMIC LEUKAEMIA

The extensive studies of Hynes have done much to indicate the place in medical diagnosis which sternal puncture and sternal trephine should properly occupy. The operation is required when examination of the peripheral blood is inconclusive for the diagnosis of leukaemia, because the marrow picture is the same whether the blood be leukaemic or aleukaemic. There is no doubt that the development of the technique of marrow examination has revealed the rarity of true aplastic anaemia and the relative frequency of aleukaemic leukaemia, especially in children in whom the initial phases may be very insidious. In childhood, any intractable anaemia accompanied by neutropenia merits a marrow examination to exclude leukaemia. Hynes states that aleukaemic phases of chronic myeloid leukaemia (from X-ray treatment and infections, and spontaneous) are common, and he claims the existence of aleukaemic cases of the same disease in which the leucocyte count is never raised. Such cases present a clinical picture of an enlarged spleen and liver, anaemia without leucocytosis and with nucleated red cells at least as numerous as primitive leucocytes in the peripheral blood. A similar syndrome and blood picture are produced by myelosclerosis. For differentiation, sternal puncture can establish a diagnosis of leukaemia and, if negative, myelosclerosis is suggested by implication. Sternal puncture in myelosclerosis is rarely successful on account of the fibrous nature of the marrow, which is only revealed in an histological section of a sample of marrow obtained by trephine. Histological section is also necessary for a confident diagnosis of aplastic anaemia.

PERNICIOUS ANAEMIA AND ALLIED ANAEMIAS

The morbid anatomy and the histology of the achlorhydric stomach characteristic of pernicious anaemia have always been a source of interest since Fenwick (1870) first described the extensive atrophy of the secretory tubules. The formulation of Castle's theory of the intrinsic factor appeared to be crowned by Meulengracht's discovery (1934) that the pig's stomach is divided histologically and functionally into two distinct parts, the fundus secreting hydrochloric acid and pepsin, and the pyloric secreting the

anti-anaemic factor Brunner's glands in the duodenum were believed to have the same anti-anaemic function as the pyloric glands of the stomach. But further work showed an apparent discrepancy when these anatomical studies were pursued in man. Magnus and Ungley, as well as Meulengracht (1939), found that, in the human subject of pernicious anaemia, the cells of the corpus of the stomach showed atrophy and inflammation whereas the cells of the pylorus and of Brunner's glands were normal. More recently Jacobson has shown that the anti-anaemic activity of the alimentary canal corresponds with the distribution of argentaffine cells. In man these cells, which contain granules that stain black with silver salts, are found in the cardia of the stomach, the pylorus, and the duodenum, and in smaller numbers in the jejunum, ileum, appendix, and even the colon. In twelve cases of pernicious anaemia examined by Jacobson these argentaffine cells were absent. Furthermore, argentaffine cells have been shown to contain a complex purine similar to one which is present in liver extract.

How far these discoveries will lead is unknown, but it is clear that a complete understanding of pernicious anaemia has not yet been reached despite the brilliant discoveries of the last twenty years.

If this be so for pernicious anaemia, how much more is it so for anaemias which are claimed to have a similar fundamental aetiology but differ as to the manner in which the essential anti-anaemic principle fails to be formed, absorbed, or used. To this class of anaemias belongs the so-called achrestic anaemia of which records of six new cases that have been extensively studied have lately been published by Israels and Wilkinson. Their studies have included examination of sternal marrow which has been found to be megaloblastic reverting to normoblastic in response to intensive liver treatment. The position of achrestic anaemia in medical opinion is still uncertain, and the disease appears now to have altered in prognosis, for none of the recently described cases has been fatal. All haematologists acknowledge the existence of this type of anaemia, resembling pernicious anaemia in its peripheral and marrow blood-picture, but differing first in that the gastric secretion contains hydrochloric acid and secondly in the very poor response to reasonable liver therapy. But, it might well be argued, if this be a deficiency anaemia and if the only method of control be intensive liver therapy, then liver extracts contain only a small portion of the deficient substance. Trial of other substances may eventually reveal a factor as potent in this anaemia as is liver extract in pernicious anaemia. Clearly there is a fallacy in assuming that an anaemia which does not respond to a given remedy is due to failure to utilize that remedy. The clinical and haematological pictures of achrestic anaemia are known and accepted, but the aetiology is still obscure.

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RECENT DEVELOPMENTS IN THE PRINCIPLES OF BLOOD TRANSFUSION

By F. A. KNOTT, M.D., M.R.C.P., D.P.H.

DIRECTOR, BACTERIOLOGICAL DEPARTMENT AND TRANSFUSION SERVICE, AND LECTURER IN BACTERIOLOGY, GUY'S HOSPITAL, LONDON

CLASSIFICATION OF BLOOD GROUPS

A change of some importance is the general adoption of the International Classification of Blood Groups which is everywhere superseding the Moss terminology. It will be remembered that if A and B represent the agglutinogens attached to the cells and α and β the corresponding serum agglutinins, the constitution and classification of blood specimens are as follows:

Moss Groups	International Groups representing agglutino-gen content of the cells	Agglutinin content of corresponding plasma
1	AB	O
2	A	β
3	B	α
4	O	$\alpha\beta$

Thus the blood of the 'universal donor' is now described as belonging to Group O. The standard high-titre sera required for blood-grouping tests are, according to the new terminology, those of Group A and Group B. Recently, during the testing of large numbers of volunteer donors, it has been noticed (Taylor, Race, Prior, and Ikin) that in some group AB bloods the A content of the cells may be relatively low and that if, when grouping tests are made, really high-titre sera are not used and the test mixtures watched for some time, the agglutination with standard Group B serum may be missed and the sample wrongly classified as Group B. Further attention has been given to the antigenic factors M and N, one or both of which will always be found in human red cells. It is now clear that although detection of these provides for medico-legal purposes a most valuable method of classifying bloods more accurately into twelve distinct groups, the corresponding agglutinins never occur naturally in human sera. Therefore, this further classification need not be considered in the selection of donors and in testing the compatibility of their blood with that of the patient. Other new points concerning the significance of blood groups will be mentioned on pp. 36 and 43. A practical point in 'grouping' is that all test sera should have an initial titre of at least 1 in 100 and to preserve this, stocks *must* be kept in the cold room. Individuals with so high a serum titre are not common and must be specially sought. With a few bloods auto-agglutination of the red cells is seen to take place at room temperature in any serum, even in physiological saline, making satisfactory 'grouping' and

'cross-matching' impossible. But if the tests are repeated at incubator temperature, 37° C, this fallacy will generally disappear.

TRANSFUSION OF LARGE VOLUMES OF BLOOD

At the outbreak of war it was already widely appreciated that up to one pint of blood could be taken from a healthy compatible donor, citrated, and at once transfused without risk to the patient. Transfusion had two objects, to make good the loss of blood or to stimulate the haemopoietic system. Essentials of the technique of a single transfusion and the general therapeutic indications were given on pp. 536 and 542 of Vol. II of this *Encyclopaedia*. At the time the object was to describe a simple method for all-round use and the two-way syringe technique was chosen. Since then a small, extremely convenient reversible rotatory pump to replace the syringe has been designed by Riddell and made by the Genito-Urinary Manufacturing Company, London, W.1. This author has also described the whole subject admirably in his recent monograph on blood transfusion. His method provides the means of either rapid or slow drip transfusion (see p. 36), as circumstances and the patient's condition may require. In severe cases transfusions of more than one pint are often necessary and at that time a point still under discussion (in such circumstances) concerned the relative merits of a series of single transfusions made at short intervals and the same amount of blood (collected from several different donors) given over many hours as a continuous intravenous drip. Opinion is still divided. The choice in any particular case depends partly upon the circumstances in which the operation is performed and partly upon the severity of the case. In practised hands the drip method can be a simple procedure but it does require the continued presence for hours of someone experienced in the method: if a nurse, she must be specially trained in intravenous work. Unless one is prepared to install a special attendant, the continuous drip method is probably suitable only in hospital or good nursing home surroundings. When a series of single transfusions is made, the operator can complete each one in, say, 45 minutes. If circumstances are not ideal, the advantage in safety and convenience probably rests with the 'series' as against the 'continuous drip.' The clinical conditions for which, given good conditions, the latter is specially suitable are as follows. The transfusion of a pint of blood into an adult of average size cannot raise the haemoglobin percentage more than about 8 to 10 per cent. In long-standing anaemia of great severity (about 20 per cent haemoglobin) when the haemopoietic functions are very depressed, so a long series of single transfusions may be required before a safe haemoglobin level is reached that a satisfactory blood picture is more conveniently achieved by continuous drip. This also applies to pre- and post-operative anaemias when the patient's haemoglobin level is extremely low and the available time is short. The continuous drip may easily be carried on throughout the operation and after it. In aplastic anaemias the patients may require repeated large transfusions to maintain life and to afford meanwhile opportunity for haemopoietic recovery. It is then often more convenient to give large continuous drip transfusions at long intervals instead of extremely frequent single ones. An important consideration is that a very slow continuous drip may be less likely than a single large transfusion to provoke recurrence of haemorrhage from an inaccessible internal site. This should be especially borne in mind when it is known that slight haemorrhage may still be taking place. The slow drip is also preferable in cases of very severe chronic anaemia, the myocardial condition being very poor and cardiac failure from circulatory overloading being a very real risk if large volumes of blood are transfused quickly. The case for the slow drip transfusion has recently been

ably set out by Marriott and Kekwick, who also point out that the actual effect of any given volume of blood, both as regards immediate rise in haemoglobin percentage and subsequent haemopoietic stimulation, can be proved somewhat greater when the transfusion is very slow. They give a useful formula for determination of the volume of blood required to produce particular effects. A haemoglobin level of less than 25 per cent is considered to indicate danger to life. 35 to 45 per cent, according to circumstances, to imply relative safety. Higher levels should be aimed at in pre-operative and various other circumstances in which further blood loss may be anticipated. To determine the volume in c.cm. of transfused blood required to give whatever rise in haemoglobin percentage is considered desirable the following calculation is made

$$\frac{\text{Percentage rise in Hb required}}{100} \times 40 \times \text{patient's weight in lb.}$$

Thus to produce a rise of 10 per cent in a 10-stone patient, the volume transfused must be $\frac{10}{100} \times 40 \times 140$ c.cm. = 560 c.cm. i.e. approximately 1 pint

CONTINUOUS DRIP TRANSFUSION

Practically all the recognized methods of performing intravenous drip transfusions of saline, glucose and saline, and gum saline, may be adapted for the administration of citrated blood. To avoid rigors, which at once interrupt administration, and therefore negative all the advantages of the continuous method, particular care must be taken that all the apparatus is chemically as well as bacteriologically clean. The settling of red cells into a compact layer tending to block tubes and needles must be avoided, either by gently rotating the reservoir at intervals or, better still, by slowly bubbling oxygen through the blood. Provision must be made to filter off any small clots which may have formed during the collection of blood from the donor. A few special points also arise about the donors used for continuous transfusion. The bloods from the different donors must be perfectly compatible not only with that of the patient, but also with each other; in other words they must all be of the same group and 'cross match' perfectly.

For *single* transfusions, when the patient belongs to a group other than Group O, the donor may be of Group O, i.e. 'universal', or belong to the patient's own group. But for *continuous* transfusion the donors should all be of the same group as the patient. In any case the reservoir must never contain a mixture of bloods of different groups. Unless the patient is of Group O, universal donors should not be used for continuous drip transfusions. The reason is as follows: it will be seen from the table on page 34 that the plasma of universal donors contains the agglutinins α and β and it has been shown (Knott and Koerner) that such plasma will sometimes agglutinate the cells of any other group in exceptionally high dilutions. Transfusion of large volumes of such high-titre plasma may agglutinate so many of the patient's own cells that reactions and haemoglobinuria soon occur and then the drip must be prematurely stopped. Such universal plasma given as single one-pint transfusions practically never causes trouble, but the situation is very different when much larger volumes are given continuously.

As regards drip transfusion apparatus so many types are now in operation as to make choice difficult. But simplicity being always an outstanding advantage two may be described briefly. The technicalities of the first are given

in detail by Marriott and Kekwick (1935 and 1937) and below a very minor modification of their apparatus is shown.

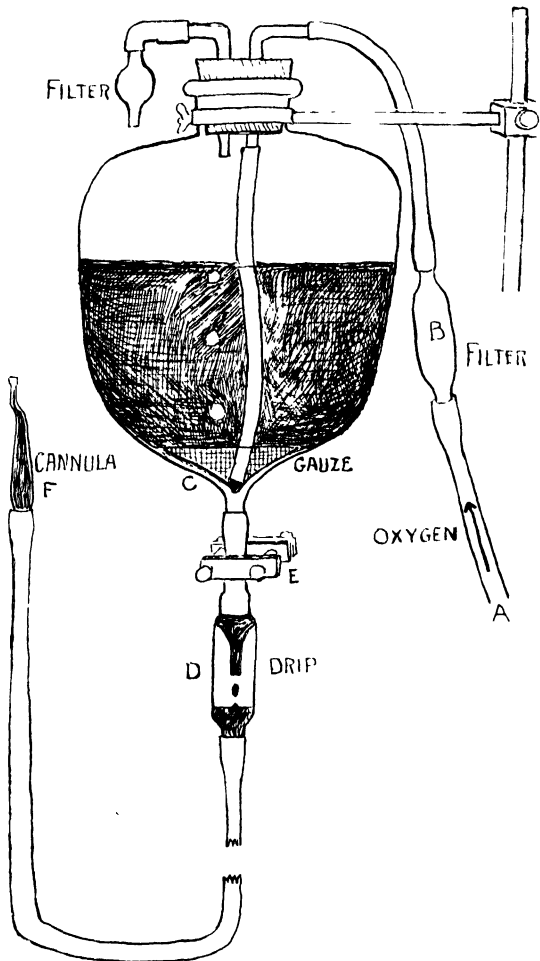


FIG. 1.—Diagram of reservoir connexions in continuous drip transfusion (from *Practical Procedures*, London, 1938).

The reservoir may be of any convenient shape provided its capacity is at least 1.5 litres. Its two-holed cork carries a tube with an air-filter and a tube through which a regulated flow of oxygen (A) can be sent at the rate of over two bubbles per second. To hold up any small clots a sterilized nickel gauze filter (C) lies at the bottom of the reservoir. The tube taking the blood to the patient carries first a regulating clip (E) and then a sight drip-feed (D). The reservoir should be supported about four feet above the patient's head. The reservoir first has a little sterile physiological saline run into it and the transfusion started with that. Blood is poured in when everything is working smoothly. Unless the patient has large veins it is best to cut down and tie in a small glass cannula (F). With larger veins a carefully inserted needle is satisfactory. But in either case a vein should be chosen well away from joint flexures and the best position is the flexor surface of the forearm. Here the cannula or needle and the last three inches of the tube can be strapped

in position and the forearm, being backed by a short splint, it and the tube can be bandaged so firmly in position that limited movement of the arm can be allowed without risk of disturbing the transfusion.

Another very satisfactory form of reservoir and delivery apparatus is that devised by MacCartney as an application of the metal screw-on, two-way top designed to fit the standard U.G.B. screw-capped bottles. A diagrammatic representation of the apparatus is given in Fig. 2. The metal two-way caps are supplied by Vann Bros., London, W.1.

In this case the flow is carried on by siphonage. At the start by gentle blowing down tube A, liquid is forced up the centre tube B and over into delivery tube C until the siphon runs. Once the siphon is started and liquid flows from the needle or cannula, as the bottle empties the clip D can be closed and the flow stopped. This done, the first bottle can be unscrewed from the top without breaking the siphon and a full one screwed into its place without dismantling anything. Releasing the clip at once restarts the siphon and the drip flows again. With this apparatus it is really unnecessary to maintain a stream of oxygen, although metal tops can be obtained with an extra tube for this purpose. Gentle agitation of the bottle at intervals suffices to keep the red cells suspended. It is usual to start the drip with a bottle of sterile saline and when this is running smoothly to close the clip, remove the saline bottle, and screw one containing the litre or so of blood into its place. Releasing the clip at once starts the transfusion. The blood can either be filtered through gauze before it is placed in the bottle or a small filter may be included at the end of tube B.

This is a particularly convenient apparatus because, provided all the solutions likely to be given intravenously to any particular case (saline, plasma, blood, etc.) are all stored in the same type of standard screw-capped bottle, these bottles can be interchanged at will at any time and without disturbing any other part of the apparatus. Only the clip has to be closed before a bottle is detached and reopened after the fresh bottle is screwed into position.

TRANSFUSION OF STORED BLOOD

Experience gained during the Spanish Civil War attracted much attention to the possibility of storage and long-distance transportation of blood for transfusion purposes (Jorda). The limitations under emergency conditions of any service based upon the personal attendance of living donors had been generally realized. In Spain the great value of central stores of blood was proved. Passing attention had been given to the collection and storage of cadaver blood (Yudin) which might be obtainable under field conditions. Similarly in civil hospitals the possibility of the collection and storage of placental blood had been tried (Goodall *et al.*). Neither had proved to be satisfactory owing chiefly to the difficulty in obtaining sufficient quantities and avoiding bacterial contamination. Some time before the outbreak of the present war a stage had been reached when it was realized that panels of healthy adult donors formed the ideal source. The only problems to be solved were the organization of systematic blood

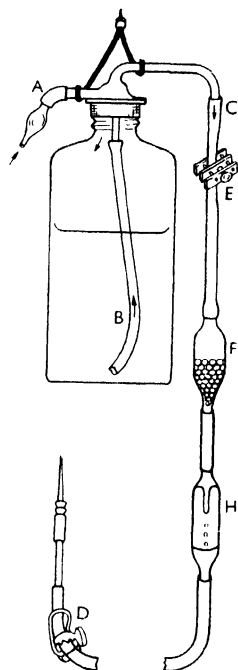


FIG. 2 MacCartney's intravenous drip. A, tube for air-entry; B to C, delivery tube passing through metal cap and providing, with rubber assembly, siphon action; D, ratchet quick-release clip; E, fine adjustment screw-clip; F, glass bead filter; H, glass drip. The bottle is suspended two or three feet above the patient's arm.

collecting stations and the exact methods by which the longest possible preservation of the blood could be achieved.

STORED BLOOD DEPOTS

In the London and Home Counties areas, under the guidance of the Medical Research Council, these questions were vigorously tackled with the result that large panels of volunteer donors were compiled and their services allotted either to specially organized depots or to some of the larger hospitals where blood could be collected and stored, the same procedure was adopted in many hospitals in the provinces. In all these instances the object of the centres has been systematically to determine blood groups and Wassermann reactions and to decide from physical examination and family history that the volunteer was a suitable healthy donor. By card-index methods complete

individual records have been kept and at appropriate intervals donors asked to visit the centre, one-half to three-quarters of a pint of blood being collected from each and stored by the methods described below. The blood was then distributed for clinical use, distances varying between those involving air or motor transport and simple conveyances from a refrigerator to a neighbouring ward. Once the establishment of such centres was decided upon, three main points had to be settled. A simple, standardized, inexpensive yet efficient collecting apparatus

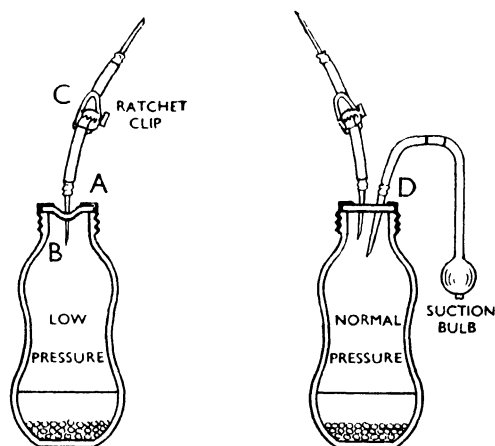


FIG. 3—Blood collection in I.M.S. bottles. With good negative pressure, the rubber cap B is found drawn inwards. If cap is flat the suction bulb must be used.

apparatus had to be evolved. A standard method of actual transfusion was less necessary as many institutions were already equipped and employed well-established methods of their own. But in this respect also the Medical Research Council made recommendations. It had already been generally agreed that citrated blood was the most easily collected and handled, so that it only remained to decide the optimal volume and strengths of the anti-coagulant solutions and those conditions of storage and transport which allowed the maximal percentage of stored bloods to be still satisfactory for transfusion by the time they reached the patient. The Council published a description of the Emergency Blood Transfusion Service Outfit in booklet form in September, 1939.

As regards *collecting apparatus*, the equipment chosen by the Medical Research Council stations was based upon MacCartney's principle of adapting the screw-capped bottle to rapid collection of venous blood.

The metal screw-cap (A) has a central perforation and beneath it a rubber washer (B). Before final sterilization of the whole apparatus in the autoclave the pure, filtered citrate solution is run into the bottles. These are autoclaved with the caps still loose so that the contained air escapes and is largely replaced by steam. When the autoclave pressure is released, the caps are at once screwed down firmly. As the bottles cool, the steam condenses

and a high negative pressure is produced inside the bottle. To collect blood from a donor all that is required is a sterilized length of rubber tube with needles at either end as in (C).

The tube is clipped in the middle, one needle thrust through the rubber cap of the bottle and then the donor's vein punctured with the other needle. On releasing the clip blood flows very rapidly into the bottle owing to the negative pressure and the bottles usually fill to within two inches of the cap. In each standard bottle about 350 c.c. of blood is collected. The method is very quick and efficient and the chances of contamination are reduced to a minimum.

Alternatives in technique are described in the publication of the Medical Research Council, but the above is undoubtedly the simplest in general use. If circumstances allow only ordinary sterilization of the collecting bottles they will carry less negative pressure. Then, after venepuncture as above, a second needle, D, connected to a suction pump may be thrust through the rubber cap and the flow of blood can be accelerated at will. This form of collection is, in fact, preferred by some because the high initial suction with 'vacuum' bottles causes distortion and some subsequent haemolysis of the red cells.

ANTICOAGULANTS FOR STORED BLOOD

The anticoagulant solution originally advised for use in the E.M.S. collecting bottles was 1.05 per cent sodium citrate in 0.85 per cent sodium chloride, both salts being of high grade purity and the water freshly distilled. After filtration, the solution was immediately autoclaved. But the above solution is hypertonic and experience showed that this could be improved upon. The general tendency of stored blood is to undergo the following changes. After the second day the sugar content falls and some lactic acid appears. The complement content gradually falls and reaches zero in about a fortnight. All red cells soon lose their reticulum and variations in shape and size appear together with marked increase in fragility as time passes. The cells slowly lose their agglutinogens and the sedimentation rate falls. The majority of the white cells lose their functional activity after a few days. Platelets gradually disappear. The greater the changes in the red cells, the more quickly spontaneous haemolysis takes place but, provided the plasma directly above the settled red cells remains amber in colour, it can be assumed that relatively few of the latter have broken up. True isotonicity of anticoagulant solution was found to result in less liability to haemolysis; the solution should therefore be sodium chloride 0.43 per cent, sodium citrate 1.05 per cent (Maizels and Whittaker). Also a slight acidity (pH 6.6) further reduces haemolysis probably by decreasing cation (sodium) penetration of the red cell envelopes. This acidity can be obtained by adding a little carbohydrate to the solution. It seems therefore that the best anticoagulant solution to use for blood storage is sodium chloride 0.43 per cent, sodium citrate 1.05 per cent, and glucose 1 per cent or dextrin 3 per cent. One volume of this solution should be used for two volumes of blood.

Even at 2° to 4° C., the temperature at which the bottles of blood are stored, chemical changes occur and according to recent observations (Aylward, Mainwaring, and Wilkinson) these seem to be (a) diffusion of potassium from the red cells into the plasma; (b) an initial fall and subsequent rise in the plasma inorganic phosphate; and (c) a gradual rise in plasma haemoglobin as the cells haemolyse. It is now agreed that addition of carbohydrate to isotonic citrate-saline tends to delay (b) and (c). Such a solution is definitely superior to heparin in this respect. Shaking the blood accelerates haemolysis and is to be avoided. Blood must never be allowed to freeze. This

causes marked haemolysis. Such blood, after thawing, is very liable to cause reactions.

ADMINISTRATION OF STORED BLOOD

Any method used for transfusing fresh citrated blood may be used for the stored blood. A layer of glass beads is generally included in the collecting bottle so that complete mixing of the cells and plasma can be obtained with the minimal shaking of stored blood; if carefully collected there are no clots. With all samples some form of filter *must* be included in the transfusion outfit, or the storage bottle being opened, the blood may be run through a gauze filter into whatever reservoir is to contain the main supply during actual transfusion.

The advent of stored blood has not been followed by any new system of administration. It is true that under the Emergency Transfusion Service of the Medical Research Council, a very large amount of equipment has been sent out to hospitals. When this is assembled, as described in the Medical Research Council's booklet, it results in an apparently straightforward method of running the blood direct from the storage bottle into the patient's vein. The simple principle is adopted of fitting the bottle with a two-holed bung carrying a long glass tube (for air entry) reaching to the bottom of the bottle and a short one from which a long rubber tube, with clip and glass drip, passes to the delivery needle and the patient's vein. When the bottle is inverted and suspended three feet or so above the patient's head the blood flows by gravity. It cannot be said that this original simple apparatus was a great success. But it was valuable in the sense that its wide-spread distribution in September, 1939, at once provided some means of giving several transfusions at once in hospitals previously unequipped in this respect. Since then a large number of suggestions have been put forward by various experimenters for making the apparatus less erratic in its behaviour and more efficient as regards filtration, rate of flow, ease of vein puncture, and so forth. The best were soon published as a summary (Vaughan), and several have been officially adopted, new sets of accessories being issued accordingly. The result is definite technical improvement. But the fact remains that the claims of this apparatus still reside only in its ready availability to so many institutions having previously no adequate equipment of this kind. There is no reason why, as a method of administration, it should supersede any of the well-tried methods when the apparatus for these is available. It has the advantage over the simple 'tube and funnel' methods that the blood is retained throughout in the bottle in which it was originally collected. All risk of contamination is thus avoided. But this carries the penalty, in any but practised hands, of several most tiresome manipulative difficulties. In sharp contrast, the collection of blood, its storage in the Emergency Blood Transfusion Service apparatus and the system of blood depots are admirably efficient. The emergency has produced a definite advance in knowledge of the best methods of blood storage, rapid collection, and systematic distribution but as yet nothing to cause alteration in the methods by which blood transfusion is customarily performed. Before use the bottles of stored blood are stood for 20 minutes in a large bulk of water at about 40° C. The temperature must never be higher. After gently inverting the bottles a few times to mix cells and plasma, the blood is then ready for administration by any of the usual methods.

REACTIONS FROM STORED BLOOD

An important point upon which an opinion can now be given is whether or not stored blood is especially liable to produce reactions. Some of the reports before 1939 suggested that after the first week of storage, the blood

often caused rigors and transient pyrexia. But since the conditions of storage have been standardized as above, and following the even more recent adjustments in the anticoagulant solutions, these reactions have become increasingly rare. From what has been said of these solutions it will be seen that improvements have reduced the degree of chemical change likely to occur in the blood and reactions have diminished accordingly. It is now rare to see reactions caused by blood after one week's storage and even with blood stored one month in the cold room they are never severe (De Gowin and Hardin). Nevertheless, it is generally agreed that one month should be the maximal time of storage. Blood in store should be inspected from time to time and those bottles showing marked early haemolysis discarded. Some gradual haemolysis always takes place, but rapid haemolysis suggests deterioration or even contamination. When the freshly collected blood is allowed to sediment for a short time at room temperature and then placed in the cold, the cells rapidly settle into a compact layer with relatively clear, amber coloured plasma above. As time passes, some haemoglobin diffuses slowly upward from the cells. The blood should never be shaken up except just before use, if it is, the cells never completely settle again, the speed of haemolysis increases, and the reaction risk rises. If transported to a distance the blood should, for this reason, be carried smoothly. The bottles should be as full as possible in order to reduce movement of the blood. At present it is customary to store both Group O bloods as 'universal donors' and Group A bloods for use when there is time to group the patients. At least 40 per cent of patients will belong to Group A and if Group A blood is used when possible, more of the universally available Group O blood will be to hand in the real emergency and when there is no time to group the patient. Although it may usually be assumed that the preliminary grouping of stored blood has been accurately done, it is well, if liability to reactions is to be absolutely minimized and if time allows, always to 'cross match' to the extent of testing some of the in-going stored blood cells against a little of patient's serum. In other respects, i.e. compatibility, allergic phenomena, and blood temperature considerations, there is no essential difference between the possible causes of reaction with stored and freshly collected blood. The latter have already been detailed in the *Encyclopaedia*, Vol. II, p. 542.

In all cases it is of the utmost importance that all apparatus for collection, storage and administration should be chemically absolutely clean—minute traces of soluble foreign protein attached to glass or rubber will cause rigors.

THERAPEUTIC EFFECTS OF STORED BLOOD

All reports show that stored blood is entirely effective in temporarily replacing lost blood and in this respect the benefit to be expected from any particular quantity is similar to that one has long been used to in the case of fresh blood. The volumes required are referred to in an earlier paragraph. It appears that the life of the stored red cells in the circulation is almost if not quite as long as that of fresh cells (*Lancet*, 1939). Haemoglobinuria is not noticeably more frequent after transfusion of stored blood. But a point still unsettled at the time of writing is the relative value of stored blood as regards stimulation of haemopoietic and antibacterial powers. Case reports are at present conflicting, personal experience would suggest that both results are powerfully produced by very recently stored blood, but its efficiency in these respects declines with the length of storage.

INDICATIONS FOR BLOOD TRANSFUSIONS AND PLASMA

During the last few years it has been realised that transfusion of plasma alone (the red cells having been removed) has definite therapeutic applications.

The indications for whole blood transfusion have been outlined in the *Encyclopaedia*, Vol II. p. 542. Those for plasma transfusion are essentially different (see below). War conditions have brought into prominence the special needs of those suffering from recent severe loss of blood, from shock, or from both. Apart from the history and any blood examinations which may be possible, the clinical points of most value in deciding that transfusion of whole blood is required are a falling systolic blood-pressure and corresponding rise in pulse rate, increasing restlessness, dyspnoea, and permanent pallor. If the patients are at the same time in a condition of severe shock which, by allowing plasma to escape into the tissues and therefore raising the haemoglobin percentage and red count, counteracts the diluting effect of pure blood loss, careful clinical examination becomes of paramount importance.

TRANSFUSION OF STORED PLASMA

In resuscitation work one or both of two distinct conditions may have to be counteracted: shock and haemorrhage. With shock alone the plasma protein content falls and the red cell count per volume rises. Haemorrhage alone causes dilution of the blood with a fall in the red count. Shock, therefore, raises the haemoglobin percentage, whereas haemorrhage lowers it. When shock and haemorrhage occur in the same patient, these effects tend to counteract each other. Nevertheless, if careful note of the clinical condition is supplemented by haemoglobin estimations, or better still by red cell counts, it is usually possible to tell which condition is predominant. Falling values indicating haemorrhage will call for whole blood transfusion. As indicated by Walther and others the rising values seen in shock are contra-indications to whole blood transfusion and are better treated by transfusion of plasma alone.

Fortunately the recent wide-spread organization for storing whole blood has made available large quantities of plasma which can be drawn off aseptically from above the level of the sedimented red cells. Although the cells are not satisfactory for transfusion after more than four weeks' storage, the plasma can still be used and after filtration remains entirely satisfactory for months even when stored at reasonably low room temperatures. Moreover, it has been found possible to dry the plasma by various means (Edwards, Kay, and Davie) and to obtain a powdered, transportable product which readily redissolves in water, thus providing a reconstituted plasma retaining all its essential properties and entirely suitable for transfusion. Dissolving the dried plasma takes, however, a certain amount of time and therefore for local emergency use the stored liquid plasma has decided advantages over the dried product; but the reduced bulk and ease of transport give dried plasma obvious advantages under field conditions. There are certain technical difficulties in obtaining a clear, filtered plasma which does not deposit fibrin on standing, thus making its transfusion difficult, but these are being overcome and bottles of stored plasma are already being distributed from the Emergency Medical Service depots.

At the time of writing attention is being directed to the red cell agglutinins (α and β) which may be present in stored plasma and liable therefore to agglutinate the patient's own cells if he does not belong to the same group as the person from whom the plasma was derived. Of necessity most of the blood stored for emergency belongs to Group O (the universal donor) and its plasma contains both agglutinins α and β often in high titre. Group O plasma quickly agglutinates the cells of all patients of Groups AB, A, and B, and although experience has shown that considerable amounts of such plasma may be given to patients of these groups without producing any untoward reactions, yet if really large volumes, as by the continuous drip

technique, are to be given it is well to mix on a slide one drop of the plasma diluted 1 in 25 with a drop of the patient's cells suspended in 3 per cent citrate solution. If no agglutination occurs at this dilution (1 in 50) experience has shown that no reactions are likely (Knott and Koerner). The ideal or 'universal' plasma for transfusion is that from Group AB which is devoid of both agglutinins and cannot therefore affect the cells of any group. But AB is such a rare group that adequate supplies of this plasma will never be available. A method of overcoming this difficulty is to mix equal parts of Group A and Group B whole bloods and allow them to stand in the cold room for a few days during which by cross agglutination each blood will take up the agglutinins in the plasma of the other. When the mixed plasma is finally withdrawn, it is free from agglutinins and equivalent to 'universal' Group AB plasma. But here again is the difficulty of obtaining sufficient Group B blood, this group occurring in only about 7 per cent of the population. Trials have therefore been made with Group A plasma which contains only β agglutinins and is obtainable as often as Group O plasma. As only one agglutinin is present, it will clump the cells of only Groups AB and B, both rare groups. The cells of Group O are inagglutinable. Group A plasma is, therefore, entirely suitable for patients of Groups O and A which together comprise over 80 per cent of the population of this country. Theoretically, Group A plasma is preferable to that of Group O. In practice it is just as easy to obtain, since Groups O and A occur with about equal frequency. Until very large numbers of cases have been treated it is impossible to be certain that administration is absolutely devoid of all risk but so far it appears that, provided the plasma is filtered, clear, and practically cell-free, reactions do not occur. The value of this form of transfusion in traumatic shock has already been mentioned. Its virtues in the case of severe burns have been widely proved and there is some evidence (Brennan) that, when whole blood is not available, plasma alone may also do much to counteract the effects of blood loss. The methods of administering plasma are essentially those available for any other form of intravenous therapy. The liability of stored plasma to produce deposits of fibrin makes it advisable to examine it carefully and if necessary to pass it through some form of quick filter before administration. Several layers of sterile gauze will usually suffice. Recently it has been found that the sedimented red cells, remaining after the withdrawal of plasma for storage, can, after gently mixing with sterile, isotonic diluents, still be usefully employed for transfusion of patients suffering from blood loss. Those cells nowadays available while they are still fresh usually belong as explained above, to Group A and their use calls for preliminary grouping of the patient, they are not 'universal donor' cells.

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INJURIES OF THE EAR

By LIONEL COLLIDGE, M.B. F.R.C.S.

SURGEON, GOLDEN SQUARE THROAT, NOSE AND EAR HOSPITAL; AURAL SURGEON,
WEST END HOSPITAL FOR NERVOUS DISEASES, LONDON

Direct injury to the ear is common in war but comparatively infrequent in civilian life, whilst indirect effects upon the ear are a frequent concomitant of the familiar types of head injury and fractures of the skull, which modern methods of transport and industrial progress have done nothing to eliminate

INJURIES OF THE PINNA

Of injuries of the pinna little need be said, except that their character is naturally influenced by its anatomical structure, that consequently haematoma, perichondritis, and deformity are liable to follow, and that there is a peculiar susceptibility to infection by the *Pseudomonas pyocanea* in addition to the common pyogenic organisms.

INJURY OF THE EXTERNAL AUDITORY MEATUS

Injury to the external auditory meatus may be caused either by a gunshot wound or by a fracture of the temporal bone, but even in a gunshot wound the extent of the injury is rarely confined to the meatus. Should this happen, however, stenosis of the meatus is likely to follow extraction of the projectile, just as a foreign body left too long in the meatus may cause excoriation and a fibrous stenosis. Attempts to relieve this stenosis by dilatation or incision are futile and painful, and it should be treated by a plastic operation similar to that employed to enlarge the meatus in the radical mastoid operation.

RUPTURE OF THE TYMPANIC MEMBRANE

Rupture of the tympanic membrane may in the same way accompany a fracture of the temporal bone passing through the capsule of the tympanum, and may be caused by a gunshot wound or by a foreign body reaching the membrane through the external meatus. In a different category are those ruptures of the tympanic membrane which occur both in military and civil practice from sudden atmospheric compression produced either by an explosion or by a blow on the pinna.

Accidental rupture of the tympanic membrane by a foreign body is generally caused by scratching the meatus with a hairpin, a tooth-pick, or a knitting needle to relieve itching. A match being blunt is a less dangerous instrument. This accident sometimes occurs also from clumsy or careless syringing of the ear, especially if the patient makes a sudden or unexpected movement of the head. The tympanic membrane is usually perforated in the anterior portion in front of the malleus owing to the direction of the meatus which the foreign body or instrument must naturally follow. There must of necessity be some damage to the middle ear, and in some instances the point of the instrument has traversed it and inflicted serious damage on the internal ear. At the moment of perforation there is a sharp intense pain, and slight haemorrhage;

should the inner wall of the tympanum or the internal ear be damaged, there may be vertigo or a severe grade of deafness. If the ear is kept dry, such traumatic perforations usually heal rapidly but, if the ear is not kept dry, as would happen from an accident during syringing, a troublesome infection and suppuration of the middle ear are likely to result. Such accidents are recorded as resulting from the unskilful use of instruments for the removal of foreign bodies from the meatus. In such cases there is always the possibility of a pre-existing suppuration, the irritation of which has induced the child to insert a foreign body, but such clumsy manipulations appear to be particularly dangerous, and may cause meningitis. Even lateral sinus thrombosis and pyaemia have been recorded (Bruhl).

Injury to the tympanic membrane by atmospheric compression is commonly caused by an explosion, but sometimes simply from a box on the ear. Eustachian obstruction or a thin scar in the membrane would dispose to rupture of the membrane in such circumstances, and a haemorrhage into the middle ear produced in this way may lead to a secondary perforation of the membrane a few days later, and so result in suppuration of the middle ear.

The rupture may be situated in any part of the tympanic membrane, except Shrapnell's membrane. In other words it is always in the pars tensa. The perforation is often oval, but it may be round, linear, reniform, or even stellate. It may be quite small or so destructive that only remnants of the membrane attached to the tympanic ring are visible. The edges are often everted rather than inverted as might be expected, so that apparently the force may act by suction or aspiration rather than by compression. Faulder called attention to this, and remarked that, when the windows of a house are damaged by an explosion, some may be blown into the room whilst others may fall into the street, so that there appear to be areas of rarefaction as well as of condensation, and perhaps also a neutral zone which would in some measure account for the different effects produced on the ear (Faulder). It is now known that the blast of an explosion produces a wave of compression followed by a wave of negative pressure, which is weaker and of longer duration (Zuckerman). It is possible that in the ear the rupture is produced by the compression and the eversion by the suction which follows. It is said that, if the explosion occurs in a confined space, the injury will probably be bilateral, whilst in the open air it will be either unilateral or at least more severe upon one side (Bourgeois and Sourdille).

Pain is severe, but does not last long, and is followed by a sharp haemorrhage from the edges of the tear. There is deafness which may be of the middle-ear type, but often there is also a disturbance of the labyrinth, so that the deafness is of internal-ear type and may be associated with vertigo and nystagmus. The rupture of the tympanic membrane, however, seems often to protect the labyrinth from the effects of the violence, and it is not rare to encounter severe damage to the internal ear while the tympanic membrane remains intact or is the site only of a few punctate or lenticular interstitial haemorrhages. It is probable that, in warfare, rupture of the tympanic membrane is diagnosed far more often than it really occurs, because, in men exposed to gunfire, bleeding from granulations or from the mucous membrane of the middle ear exposed through an old perforation is common (Colledge).

Such injuries of the tympanic membrane can heal with recovery of the hearing power, but an adhesive otitis may be caused and, if infection supervenes, which is not infrequent, a chronic suppurative otitis may result which is often resistant to treatment. If the ear is kept dry and protected as far as possible from external infection, the prognosis is good, but it is always uncertain apart from the possibility of concomitant damage to the internal ear. The question sometimes arises later whether a perforation with chronic

suppuration of the middle ear is of traumatic origin. This may be impossible to decide unless the history is quite certain or unless the ear has been examined before the injury occurred. The only cases in which it can be decided with certainty that the suppuration is not of traumatic origin are those in which the perforation is in Shrapnell's membrane. Such cases of attic suppuration are not infrequent in soldiers, because the hearing is often well preserved and the amount of discharge small. Thus there may be much destruction in the attic with symptoms at first so slight and insidious that attention is not drawn to it. A study of direct injuries to the ear and of fractures from firearms was made by Le Mee, and Passow published a book on injuries of the ear, in which are described the gross characters of injury produced by firearms and fractures of the skull.

The war of 1914-1918 provided the clinical material for much further study, but direct penetrating wounds of the mastoid process and middle ear are not common in warfare. Portmann made a study of 42 cases of gunshot wounds of the ear seen in the clinic of Professor Moure at Bordeaux. In 14 cases the missile was in the tympanum, in 21 in the mastoid, and in 7 in the petrous. For the extraction of such foreign bodies the exposure provided by the radical mastoid operation is usually the best method of approach, and it also enables rough or splintered bone to be removed. Apart from intracranial infections, the complications most likely to be troublesome are facial paralysis and ankylosis of the temporo-mandibular articulation. Wounds of the great vessels, the internal carotid, and the lateral sinus are rarely seen, no doubt because they would be rapidly fatal. Dickson recorded the case of a sailor who was wounded in the mastoid process by a bullet which was found lying in the lateral sinus where it had produced an aseptic thrombosis.

Physiology of Eustachian Tube

Aviators are naturally subjected to rapid changes in atmospheric pressure during ascent and descent. The action of these changes of pressure on the tympanum is normally compensated by ventilation through the Eustachian tube whereby the pressure in the middle ear is equalized with the atmospheric pressure.

The physiology of the Eustachian tube under these conditions has been studied experimentally by Armstrong and Heim. The investigations were made on five healthy men subjected to changing rates of pressure varying from 5.4 to 27 mm. of mercury per minute, corresponding to 200 to 1,000 feet of altitude per minute, through ranges of pressure from 760 to 141 mm. of mercury, corresponding to 0 to 40,000 feet in altitude. By decreasing the pressure from sea level at a constant rate it was found that a change of 3 to 5 mm. of mercury, or 110 to 180 feet in altitude, was required to produce any effect. The discomfort increased until at 15 mm. of mercury, or 500 feet in altitude, an involuntary click was felt in the ear and the sensation of fullness was relieved. Succeeding clicks occurred at intervals of 11.45 mm. of mercury, or 435 feet in altitude, the succeeding clicks during ascent corresponding rather to the changes in altitude than to identical increases in rarefaction. When the atmospheric pressure was increased, as it would be in a sudden descent, a totally different effect was obtained. The Eustachian tube remained closed under all degrees of pressure, and finally the tympanic membrane ruptured, unless the tube was opened by a voluntary act of swallowing, which becomes impossible when a negative pressure of 80 to 90 mm. of mercury is produced in the middle ear.

In actual aviation the capacity to compensate for these changes by opening the Eustachian tube is important, and any tubal catarrh or stenosis which prevents this may cause acute congestion of the tympanum or even rupture

of the membrane with symptoms varying from deafness with vertigo and tinnitus to sudden acute pain with the sensation of a blow followed by nausea and collapse in the case of rupture. But, if a negative pressure in the middle ear beyond 80 to 90 mm. of mercury is produced, the Eustachian tube cannot be opened voluntarily and relief, short of rupture of the membrane, can only be obtained by returning to a higher altitude. The damage to the ear in these circumstances is described as *acute aero-otitis media*. The discomfort and deafness with retraction and stretching of the membrane caused by repeated experiences of this kind is called *chronic aero-otitis media*.

Apart from effects of this kind upon the middle ear, workers in compressed air may develop labyrinthine symptoms amongst other manifestations of caisson disease soon after decompression. There is a sudden onset of vertigo, tinnitus, and deafness. Recovery may be complete, but, according to Bertoin¹ there may be permanent loss of function both cochlear and vestibular.

FRACTURES OF SKULL INVOLVING THE EAR

Although fractures of the skull involving the temporal bone are sometimes limited to the external auditory meatus, to the mastoid process, or even to the walls of the tympanum, by far the most important are those which pass through the petrous portion. Statistics showing the proportion of cases in which the petrous portion of the temporal bone is concerned in fractures of the skull vary very much and are probably misleading, but it is fairly high, perhaps in about one-quarter or even more. The cause is usually a blow or a fall on the head, and less commonly the violence may reach the skull indirectly from a fall in the sitting position or on the chin. The fracture of the petrous, however, is always indirect and reaches it by irradiation, though rarely the petrous alone is fractured. It is now, however, considered that these independent fractures of the petrous are more common than was formerly believed. But usually the fracture radiates from some part of the vault into the anterior, middle, or posterior fossa. The line may not extend beyond one fossa or it may cross the buttress of the great wing of the sphenoid or the petrous into a neighbouring fossa. Although the petrous appears to form a solid buttress, it is less strong than it appears because it contains the cavities in which the organ of hearing is lodged. The petrous may thus be reached by a fracture from the temporo-parietal region crossing the middle fossa and producing a longitudinal, and rarely a transverse, fracture, or secondly it may be reached from the occipital region across the posterior fossa so that a transverse fracture is produced or the tip of the petrous broken off, or the fracture may be oblique. Of these three varieties of fracture of the petrous—longitudinal, transverse, and oblique—the longitudinal is the most common, exceeding in frequency the transverse and oblique combined. It is impossible, however, to fit every fracture into such a rigid classification, for the line or lines of

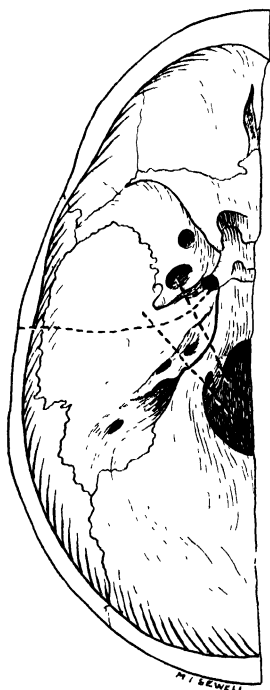


FIG. 4. To show the direction of longitudinal and transverse fractures of the petrous portion of the temporal bone

the fracture do not in every case follow the typical route, and the classification is only schematic, though most cases conform to it. There is also another fracture of great importance in the present connexion, namely fracture of the bony labyrinth which can only be demonstrated by the microscope.

In the longitudinal fracture of the petrous the line runs down from the squamous portion of the temporal bone or from the parietal bone just behind. In the first case it crosses the external auditory meatus and the tegmen tympani. In the second case the line first crosses the upper part of the mastoid process and then reaches the tegmen. From the tegmen the line follows the anterior aspect of the petrous pyramid to the depression for the

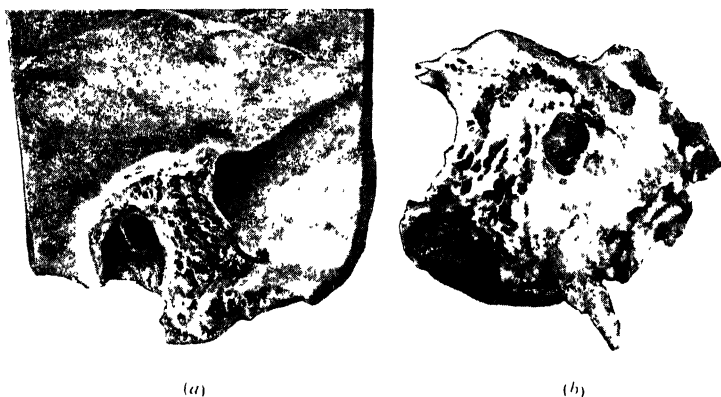


FIG. 5. Fracture of the 'lid' of the right mastoid antrum. (a) The medial aspect of the lateral segment of a right temporal bone is shown with a complete separation of the lateral wall of the mastoid process, in one piece, down the line of the squamomastoid suture. The cartilaginous portion of the external auditory canal has been torn away from the osseous portion. (b) The lateral aspect, the 'pneumatic' mastoid process has been split along the squamomastoid suture, exposing the mastoid antrum and the tympanic attic. The head of the malleus and the body of the incus are seen above the unruptured membrana tympani. (From *Lancet*, 1939)

Gasserian ganglion along the upper wall of the Eustachian tube and the carotid canal.

The petrous is thus divided into two unequal parts, an anterior which includes parts of the external auditory meatus and of the middle ear, and a larger posterior portion which includes the aqueduct of Fallopius, the internal auditory meatus, the whole of the internal ear, and part of the middle ear. Thus the middle ear is always involved in the fracture, and the tympanic membrane is torn in almost every case. On the other hand the internal ear remains intact and the facial nerve usually escapes.

In the transverse fracture, which follows a blow on the occiput or the mastoid region, the line passes forwards across the petrous somewhere in its middle third at right angles to the long axis, starting from the jugular foramen. This track may pass across the internal auditory meatus, so catching the internal ear, to the foramen spinosum, or may lie more externally and pass right across the labyrinth and the aqueduct of Fallopius. In the latter case the internal wall of the middle ear is fractured, but in neither case is the tympanic membrane torn. On the other hand the facial nerve is likely to be injured either at the internal auditory meatus or in the aqueduct.

Thus in the typical longitudinal fracture the membrana tympani is torn and

the middle ear opened, whereas in the transverse fracture the tympanic membrane remains intact, but the facial nerve is liable to injury and the labyrinth is fractured.

The oblique type of fracture is caused by a blow on the occiput. It starts from the most postero-external part of the petrous, or the posterior surface of the mastoid process in the neighbourhood of the lateral sinus, and passes forwards and inwards. The line of fracture thus includes the mastoid process, the posterior wall of the meatus, the tegmen tympani and the middle ear, the internal ear and the aqueduct. The tympanic membrane is torn, and this type of fracture combines therefore the principal characters of both the longitudinal and the transverse fracture.

In exceptional cases which do not fall within these three categories atypical fractures have been reported, such as one described by A. H. Cheatele, in which the line of fracture taking a curved course cut off the middle ear, the external auditory meatus, and the outer wall of the antrum from the rest of the petrous. Pringle states that he observed 4 cases of this fracture, which came to autopsy in a series of 366 cases of undoubted fracture of the skull under his care. He thinks that this kind of fracture, which is not usually described, is not very rare, as he believes that it occurred in 11 more patients in the series, who recovered.

Of great interest is the microscopical fracture of the labyrinth, the existence of which has long been suspected and has now been proved by pathological study of temporal bones. These fractures, which are not visible to the naked eye, may be seen by radiological examination, but their existence can only be proved satisfactorily by the microscope. The fracture may be of the transverse type, or entirely confined to the labyrinthine capsule. The site of election for such fractures of the capsule is at its weakest part in the region of the oval and round windows; the thin bridge of bone between them is fractured, possibly also the foot-plate of the stapes, and the membrane closing the round window is torn. The foot-plate of the stapes may be broken into fragments which override one another or become comparatively widely separated. The line of the fracture may spread inwards across the cochlea to the internal auditory meatus. On the other hand the fracture may consist, as Nager has shown, of a number of fine complex tracks which break up the capsule of the labyrinth, like a crushed egg-shell.

The old observation of Malgaigne that fractures of the skull unite slowly and by fibrous union only has been proved to apply to these fractures of the labyrinth. This defective repair carries with it special and remote dangers in the region of the middle ear, because the fibrous scar, which is weak or may scarcely exist at all, forms an ineffective barrier to the spread of an infective process. This relationship between labyrinthine injury and late meningitis has been studied particularly by Nager. In the cortex of the petrous the fracture unites by solid bone, but in that part of the labyrinth which forms in the inner wall of the middle ear, that is the promontory and the region of the oval and round windows, there is fibrous union only; there may even be gaps in this, and the fragments of the stapedial foot-plate may remain separated without any attempt at repair. Nager has been able to demonstrate, by histological sections of the temporal bone from a patient who died from meningitis six months after a head injury, the passage of inflammatory granulation-tissue and leucocytes from the middle ear to the cochlea through a defect in the promontory. Nager has shown also that the labyrinthine capsule consists of three layers. An endosteal layer of embryonic bone forms a thin lining to the cavities. A periosteal layer of diploetic bone capable of repair by bony union is relatively thick in the neighbourhood of the dura mater, but deficient in the region of the promontory and the two windows.

Between these is an enchondral middle layer. This enchondral layer does not undergo the process of growth and ossification which proceeds normally in other parts of the skeleton. In the labyrinth it remains permanently in an embryonic stage, immune from the ordinary processes of absorption and regeneration, and equally immune from senile osteoporosis, but also lacking the capacity of repair. As this layer forms almost the whole thickness of the bone composing the promontory and the area around the windows, an explanation is provided for the curious phenomena exhibited by the fractures under consideration.

It appears from this that a longitudinal fracture, which lays open the tympanum and exposes it to infection, carries with it some immediate risk of meningitis or other intracranial complication, but remote risk of this kind is small. On the other hand transverse fractures or any other unclassified form of fracture which occasion a fracture of the labyrinth, without necessarily being accompanied by a rupture of the membrane, induce a permanent liability to meningitis from a chance attack of otitis media which finds no resistance offered to an immediate invasion of the labyrinth. Thus Schlittler recorded a case in which, after a head injury, the caloric reaction disappeared entirely on one side, but some power of hearing remained. Sixteen years later a very slight attack of otitis media was followed by meningitis which proved fatal, and histological examination revealed a fracture of the labyrinth which was responsible for the meningitis. Ramadier collected the following records, some of which had already been noted by Nager, of this kind of late meningitis: 4 weeks (Scherbe), 4 weeks (O. Voss), 6 weeks (Politzer), 7 weeks (Klestad), 6 months (Nager), 7 months (Rynter), 15 months (Ramadier), 15 years (Brocq), and 16 years (Schlittler). The necessity for a guarded prognosis in such cases, and the possible medico-legal implications, are apparent.

Examination of the ear in head injury should follow the usual lines, but all syringing or lavage to clean the external auditory canal of blood clot or other debris must be avoided. The membrane may, according to the nature of the deeper injury, be normal in appearance, may be torn and bleeding, or less frequently may be intact but swollen and deep purple from an effusion of blood into the middle ear. In this case the blood may escape by the Eustachian tube into the nose or the pharynx. The escape of cerebrospinal fluid from the ear is a well-known sequel. It indicates a rupture of the meninges and the tegmen, and clearly indicates the possibility of meningeal infection, but it is not necessarily fatal. It is also not necessarily associated with rupture of the tympanic membrane, as the fluid may escape by a fissure in the tegmen or it may fill the spaces of the middle ear without escaping by the meatus. Voss described 6 cases of this peculiar phenomenon under the title of 'Liquor tympanum'. In this case examination of the ear shows the membrane bulging without discoloration and sometimes exhibiting a fluid level.

The usual functional examination of the ear should also be made as far as possible, but too much emphasis is sometimes laid upon this, as the general condition of the patient often prevents the examiner from making sufficiently accurate observations to be of any clinical value.

Treatment as a rule follows the general lines of treatment in head injuries, and operation on the ear is seldom indicated. For the last thirty years, however, Voss has persistently advocated systematic operation when there is evidence of fracture of the petrous. He has long held that in such circumstances the radical mastoid operation should be performed, all clot, splinters and rough edges of bone removed, the track of the fracture followed, and if necessary the labyrinth opened. He has no doubt carried this opinion further than is justifiable on the analogy of the operative treatment required for

fractures of the cranial vault, and has had but little following or support. On the basis of the pathological observations mentioned above this method of treatment does, however, require serious consideration in special cases, especially since the control of infections by chemotherapy has so much improved the prognosis of meningitis.

Nager has expressed the opinion that in a case of old head injury with signs of fractured petrous shown by deafness, absence of vestibular excitability, intact tympanic membrane and radiological evidence of fracture in a film taken in the Stenvers position (this is with the film lying parallel to the long axis of the petrous), the earliest suspicion of meningitis calls for the radical mastoid operation and exposure of the labyrinth. This is a good guide in a situation of which the dangers are not generally appreciated.

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MENTAL DISEASES

By R. D. GILLESPIE, M.D., F.R.C.P., D.P.M.

Physician in Charge, Department of Psychological Medicine, and Lecturer
in Psychological Medicine, Medical School, Guy's Hospital, London

RECENT TRENDS IN RESEARCH

As might have been expected from the developments of the past few years, recent work in psychological medicine shows a preponderance among aetiological researches of work in the physiological field. It seems not improbable that the major discoveries and formulations of a strictly psychological kind have already been made, and that our deeper comprehension of mental disorders, especially of those conventionally called 'psychoses', but to a lesser extent of psychoneuroses as well, will depend on the result of physiological and biochemical research. The work of Gjessing, now some years old, shows an apparent parallelism in a certain schizophrenic syndrome between the quantity of stored nitrogen and the mental condition, and the modification of both by the administration of thyroxine. More recently Richter described an analogous situation following parathyroidectomy. In his patient the ensuing cyclical mental condition disappeared with calcium medication. The possible significance of Richter's observation is emphasized by his parallel experiments in animals; he found, for example, that parathyroidectomized monkeys exhibited a similar 40-day cycle of activity. When it is recollected how many mental conditions follow a cyclical or at least a recurrent course, how, in depressions, for example, a single day's cycle may epitomize the whole course of the illness, and how seldom biochemical investigation has tried to follow the cycle throughout, investigators being too often content with isolated measurements, it will be realized that these results are stimulating, not only in themselves but for what they may foreshadow. It is unwise, however, to deduce a great deal from them, as they concern admittedly rare conditions.

Toxic amines and hepatic disorders

Although it is only recently that biochemical and experimental investigations have been extended with something like success to these physiological anomalies, they have for a much longer time been concerned with pathological conditions produced by external noxae, usually so-called 'toxins', but such researches have not until recently borne the real imprint of scientific work.

Lately, however, the auspices in this field have been better. Partly under the stimulus of old hypotheses and partly as the result of observation of the experimental psychoses produced by mescaline, the effects of which show such striking analogies with the symptoms of schizophrenia, studies have been made, first of the effects of amines (of which mescaline is one) on brain tissues *in vitro*, and then of the possibility of such amines passing the liver barrier under certain conditions of impairment of liver function. In this connexion, Quastel and Wales had some time ago shown that such amines interfere with oxidation in brain cells, and more recently that the liver may in certain conditions, e.g. catatonia, fail to detoxicate such substances as hippuric acid. Assuming therefore that toxic substances succeed in penetrating the gut wall

at the same time as liver function is impaired, then on reaching the brain by way of the blood stream, mental symptoms might be produced (taking this evidence as a whole). One of the difficulties of this conception hitherto has been that the known effects of depriving the brain as a whole of oxygen have been very different from the symptoms of the psychoses that the view is advanced to account for, since such effects are of the type known as acute organic reactions, or less accurately, as 'confusional', whereas the symptoms in question have been of a schizophrenic or purely affective order. But the experiments with mescaline suggest either that certain amines have a specific effect in addition to the anoxic one; or that the effect of depriving certain groups of cells of their oxygen in a 'molecular' fashion, as it were, may be different from the massive deprivation that occurs from reducing the oxygen supply to the brain as a whole.

Other tests of liver function have confirmed the findings of Quastel and Wales for catatonic schizophrenia and depression with catatonic features (Berkenau). This led to some tentative therapeutic suggestions, on the ground that anything that helps the liver to excrete toxic products, may also be helpful in the cure of psychoses. Such substances, however, are still of dubious efficiency even for the local purpose.

ENDOCRINOLOGICAL RESEARCHES

The hoped-for results of the cruder type of endocrine therapy that characterized the earlier attempts to apply endocrinological discoveries to mental disease did not ensue, and the failure resulted in what may yet turn out to have been the premature discredit of this general mode of treatment. It will have been observed that both of the biochemical observations already noted, those of Gjessing and of Richter, are closely concerned with endocrine function, namely, thyroid and parathyroid function respectively. Moreover, the substitute of purer and even of artificially synthesized hormones for the older preparations - dried extracts and the like - administered, moreover, by routes and in quantities permitting them to have their physiological effects without a doubt, provides opportunities that may yet prove fruitful. It is true that the results in which these advances have been utilized, especially in the involutional melancholias of women, have so far been anything but convincing. Claims of success have, of course, been made, but, as usual in the early stages of medical experience in any therapeutic field, with no regard for simple statistical principles or even for logical errors. The chemical achievements that now render possible the accurate assay of hormone production in a given patient provide further chances for more accurate work; but even this opportunity is apt to be abused. For example, if a female patient near the menopause shows the usual changes in hormone excretion which occur at that period, and is at the same time suffering from a mental disorder, it is not really logical to recommend that she be given oestrone with the idea of restoring the hormone balance to what it would be in a still normally menstruating woman. In the meantime, it is sufficient commentary on some of the investigations in this domain to note that, while one group of investigators claims results in the treatment of involutional melancholia in women by injection of oestrone, another group shows that in women with this disease there is no quantitative abnormality in the excretion of that hormone. Nevertheless, the possible relations between the reproductive hormones and mental disease provide a tempting field of study, if only because of the traditional associations. The recurrent nature of the hormonal changes in women and the undoubted relations in many cases to changes in the intensity of mental illness are additional considerations. The phasic

alteration in the mental state in the course, say, of a depression corresponding with the phases of the menstrual cycle can be clinically very striking. It is now conceivable that this may be connected with the state of the cerebral circulation since it has been shown by Reiss and Golla that the administration of sex hormones increased the blood content of the brain in castrated young rats, and in adult rats, and that there was a similar increase during oestrus. It is still a far cry from rats to men and women, but these observations give a rather more than hypothetical basis of explanation for changes in the intensity of mental illness that have long been noted, but have remained mysterious as to their causation.

THE CEREBRAL CIRCULATION AND MENTAL DISEASE

It seems not improbable that the diameter of the cerebral blood vessels plays a larger part in the production of symptoms of mental disease than at one time seemed likely. For one thing, in this way alone it is easy to explain the comparatively rapid changes that may occur in mental illness and the *restitutio ad integrum* after a period so long that any actual cellular alteration would be likely to have left the realm of the functional and reversible and become irreversible and structuralized. Previous observations on the capillary bed in schizophrenics and Potzl's observations on the constriction of the cerebral arterioles in catatonia, support the general conception that the cerebral vascular network may prove to play a larger part in psychiatric symptomatology than has hitherto been supposed. Cotton, Lewis, and Egenhofer have recently brought additional evidence by showing that the retinal vascular bed is small in schizophrenics who do not improve, or who deteriorate; while those who improve or recover have a significantly larger vascular bed. The clinical effect of benzedrine, although disappointing from a practical standpoint, supports the same thesis of relation between mental symptoms and cerebral vascularity in a general way, since benzedrine produces an increased blood flow through the brain. The therapeutic effect of leptazol (cardiazol, metrazol) might superficially be supposed to depend on some kind of vascular effect, since the changes in heart rate and blood-pressure as well as in respiration and blood gases are sudden and profound during a convulsion (Lougheed and Hall). The vascular condition accompanying the convulsion appears to be vaso-constriction, but other evidence suggests that the effect is not through the circulation but a direct one on the cell.

VITAMINS AND MENTAL DISEASE

Considerable attention has been paid recently to this topic, the vitamin chiefly concerned being the complex vitamin B. Its established relation with nerve metabolism has led to its being employed in various psychoses. The most conspicuous success has been with the P-P fraction in the treatment of the mental symptoms of pellagra; but it has also been employed in other syndromes of the acute organic type with success, it is claimed, in delirium tremens, and in other confusional psychoses, even those of senility. It must depend for its effect on its influence on cellular metabolism, and these observations fall into line with the general trend of recent researches in the physiology of mental disease, which appears to concern itself more and more with the individual brain cell, especially its nutrition in the wide sense.

GENERAL STATISTICS OF MENTAL DISEASES

Dayton analyses the statistics derived from the examination of 89,190 admissions to mental hospitals in Massachusetts in the course of seventeen years. One of the more striking statements is that mental disorder in

Massachusetts rose during the 1914-18 war, after America's entry. This is in curious contrast to what happened in Great Britain during the years 1914-18. There was a further increase after demobilization, but a remarkable fall during the prohibition years which, however, coincided with a time of maximal employment. The decrease was most pronounced in the alcoholic group of psychoses, but there was also a distinct fall in involutional psychoses, and in 'dementia praecox'. From 1923 to 1929 there was a rise in admissions remarkably congruent with an increase in unemployment. There is some evidence that unemployment benefit also relieved the mental hospitals. Males were more affected than females by the trade depression, judging by mental hospital admission rates. The psychopathic group was affected by economic stress to a greater degree than any other, and was little affected by the war or prohibition.

The incidence of mental disease is found to increase constantly with increasing age of the population. It is suggested that it would be more appropriate to classify mental disease according to age than by any other method.

An interesting side of the book describes the statistical results connecting marriage and mental disease. Widowers exceed married men in the rate of affection with mental disease by 130 per cent, single men exceed married men by 200 per cent, and divorced men have 400 per cent more mental disease than shown by married men. As regards sex differences, single men exceed single women in mental disease by 60 per cent. Divorced and widowed males show more mental disease than females in a similar state. It is suggested that, contrary to a popular belief, marriage 'protects' the male more than the female, he is more often mentally ill if he does not marry, and also if he is so rash as to abandon marriage.

The fact that the incidence of mental disorder at older ages is increasing is correlated with the increase that is taking place in physical diseases in persons over 50, especially in cerebral arteriosclerosis. On the other hand, it is encouraging to find that mental illness at the younger ages has recently been decreasing. Moreover, readmissions have also been diminishing in recent years, and the author ascribes this to increasing efficiency of treatment in the earlier attacks. In contrast again to ordinary impression it is found that the divorce rate is high in the economically dependent group, and lower in those who are financially well provided for.

The general conclusion is reached, that there has been a slight rise in mental disorder as a whole; but a serious problem of accommodation is produced by the chronicity of so many mental illnesses, especially at later ages, and by the fact that the average duration of stay in hospital is lengthening.

TREATMENT OF AFFECTIVE DISORDERS BY CONVULSIVE THERAPY

The evidence that affective disorders can be influenced by convulsive therapy continues to grow. A manic phase can be terminated, although it tends to recur soon after, and a depressive illness can be interrupted. It now appears that it is the involutional melancholic type of illness that is as apt to be benefited as any. Bennett has increased the number of his original observations to 61 depressions and 9 cases of mania. Of the depressions, 59 made at least a social recovery, and of the manias, 8 did so. In 562 cases of affective disorder collected from the literature by Menninger 63 per cent were at least 'much improved'. This is much better than the results obtained in large series of schizophrenic cases, although the treatment was originally introduced for the latter, but inferior to the results claimed in schizophrenia by Meduna, the

originator of this method. A social recovery rate of 15 out of 19 cases is representative of the results obtainable with involuntional melancholia (David C. Wilson). Such results are so definitely better than the usual expectation in patients with involuntional melancholia not so treated that they suggest the desirability of using this method as soon as possible after the diagnosis has been made, since not only is the prolongation of suffering endured even by the ultimately recovering case prevented but the danger that the chronic habit-formation involved in the involuntional melancholic process, whatever its fundamental nature, may become irreversible is evidently also averted.

Prognosis in schizophrenia treated conservatively contrasted with the results of convulsive shock therapy

Considering all types of schizophrenics together, with a duration of illness up to several years before admission, the collation of 2,575 cases from seven different mental hospitals and clinics—six in the United States of America and one in England (Rupp and Fletcher) shows that of cases treated by the older, conservative methods, 16 per cent were much improved, 16 per cent improved, 49 per cent unimproved and the remainder dead, after a period ranging from one to ten years after admission and, in all hospitals but one, from at least two years after admission. These figures for 'spontaneous' recovery compare well with the data quoted in last year's 'Survey' from Ross and Malzberg's paper, which showed that, of over 2,000 cases treated by insulin, 11 per cent recovered (of whom 5 per cent relapsed) while 26.5 per cent were much improved (of whom some went on to complete recovery). But the two sets of figures are not strictly comparable, because Ross and Malzberg's figures referred exclusively to State Hospital patients. Their data should be compared with 1,249 of the 2,575 cases referred to above, of whom 13 per cent were 'much improved' and 16 per cent improved (Improved here seems to mean able to make some sort of social and work readjustment, and probably corresponds to Ross and Malzberg's 'much improved'.) From this data it is difficult to see any very striking advantage in the ultimate results from insulin treatment, but what is impressive about insulin (and about convulsion therapy also in schizophrenia, to a lesser extent) is the immediacy with which improvement follows on the treatment.

Mechanism of insulin shock and of convulsions

This is supposed in both types of therapy to be fundamentally connected with cell oxidation. Thus it is conjectured by some that the therapeutic effect of convulsion therapy depends on the anoxia that accompanies the convulsions (Giellhorn). With insulin, it is believed that there is a decrease in the oxygen intake by the brain-cells during hypoglycaemia, as inferred from the variations in the oxygen content of the blood in the internal jugular vein. Moreover, the electrical activity of the brain as indicated by alpha waves diminishes and disappears during the period of suppression of cortical function (Himwich *et al.*). The histologists' opinions that have been recorded, to the effect that cell-damage after repeated insulin dosage may be interpreted as due to anoxia, are in tune with this conjecture.

Technique of convulsion therapy

To overcome the disadvantages produced by the state of fear that in many patients precedes the cardiazol convulsion, and which, according to Cook, is of no therapeutic significance, various measures have been suggested including the use of an anaesthetic immediately beforehand, e.g., cyclopropane or nitrous oxide, the anaesthetic being given to a point where the lid reflexes

are abolished, and discontinued as soon as the needle of the syringe containing the cardiazol solution has been inserted in a vein. The optimal time for an injection is considered to be, in the case of cyclopropane, when the patient first moves his eyelids either spontaneously or in response to a command; with nitrous oxide the optimal point is slightly later (Neustatter and Freeman).

Picrotoxin and ammonium chloride in a 5 to 10 per cent solution have both been used as alternative methods for producing convulsions. Nitrogen inhalation has also been used (Alexander and Himwich). The principle is the production of anoxaemia by getting the patient to breathe an atmosphere with a very high nitrogen content for a maximal period of six minutes. Promising results are claimed. The method is dangerous, even in the hands of an experienced anaesthetist.

The most promising advance in technique in this field has been the electrical method introduced by Italian authors. A current is passed through two electrodes, one being placed on the fronto-temporal region on each side, over the region of the superior frontal gyrus (region 6 α/β). It is claimed that the patient always has complete amnesia for the procedure. The current, the voltage of which is adjusted to the resistance of the individual patient's head, is allowed to pass for only a fraction of a second (from one-tenth to one second). The necessary voltage varies between 80 and 250 volts, with an amperage of about 300 milliamps. It is claimed that the method is safe, but it is still in an early stage of trial. It was introduced by Cerletti and Bini and the technique has recently been described by others (Heming, Golla, and Walter). If this method proves as effective as cardiazol, its success will also be of theoretical importance, since the convulsions alone are necessary to produce the result. The immediate practical advantages are that the patient has no aura of fear or of any other kind, and that dislocations and fractures are almost unknown. In this connexion it is noteworthy that the reports of fairly frequent vertebral fractures in cardiazol convulsions, as high as 40 per cent of cases, may prove to have been much exaggerated, since routine radiological examination of the spinal column before treatment fairly often reveals appearances that might be mistaken for fractures (T. Tennant, personal communication). To limit the possibility of fractures ensuing, curare, which paralyses nerve endings and so makes convulsions less severe, has been employed beforehand (Bennett).

Complications of cardiazol therapy

The data that accumulate in this direction are on the whole not of alarming significance. Thus, although in convulsive doses cardiazol may produce disturbances of rhythm such as bradycardias, tachycardias, coupled beats, extrasystoles, and inversion of the P wave, as the result, it is alleged, of cardiac anoxaemia, no permanent ill-effects have been observed by Rankine Good, who has ventured to give cardiazol in convulsive doses to patients with various physical conditions, such as bronchitis, myocarditis, and marked arteriosclerosis, without unfavourable ultimate effect.

Later after-effects have been described but are uncommon, the most serious being pneumonia and pulmonary abscess, possibly from aspiration during the convulsion, or from small emboli detached from a vein thrombosed at the site of injection. In some instances lasting unfavourable mental effects have been noted in unsuccessful cases, the patient being more difficult afterwards (Kennedy).

Sodium amytal as a prognostic aid

When the intravenous injection of a dose of sodium amytal insufficient to produce unconsciousness is followed by clinical improvement, the chances

are greater of insulin shock and convulsion therapy (whether in schizophrenics or in depressions) being effective than if sodium amytal had no such effect (Harris *et al*)

TREATMENT OF GENERAL PARALYSIS OF THE INSANE

Kawamura and Ueda, in Japan, have recently used a virus of rickettsia type (*Rickettsia tsutsugamushiorientalis*) in the treatment of general paralysis of the insane. The virus is inoculated intramuscularly in an emulsion of testicle in Ringer's solution from a rabbit infected with the virus, or alternatively with 3 to 5 c cm. of blood from an infected patient collected during a febrile period. In 19 cases there were 8 recoveries, 9 incomplete remissions, 2 unchanged, and 1 death occurring long after the treatment. Of the cases, 14 showed a return to a normal cell-count within eleven months, 5 showed a diminution in the strength of the Wassermann reaction, and 2 became completely negative serologically. The series is small, but so far as they go the results compare favourably with the 30 per cent remissions commonly claimed for the average series treated with malaria. Moreover, the authors consider that the dangers are much less. There is the additional advantage that, unlike the plasmodium of malaria, the virus can be cultivated outside the body, and mutual infection does not exist. If these claims are confirmed by the results of treatment of a large number of cases, then an advance will have been made in convenience and safety, but whether any method which involves infection by a virus will survive the increasing use of the more controllable method of producing pyrexia by diathermy, remains to be seen.

GENETICS OF HOMOSEXUALITY

A piece of investigation that should be better known in this country was published last year by Lange on the genetic relations of homosexuality. He showed that, in the families from which homosexuals come, males exceed females in the ratio of 4 to 3; this excess of males occurs in the male line, and when the homosexual is one of twins the other member is significantly often of the same sex. All this evidence points to a constitutional, possibly ultimately hormonal, basis for some cases of homosexuality. In others it is without a doubt predominantly psychologically determined, but these facts could well be remembered in connexion with psychotherapeutic prognosis.

PSYCHIATRIC EXAMINATION OF CASES OF BRAIN INJURY

Great difficulty has been experienced in discovering tests of disorder at the highest level of thinking. Intelligence tests of the ordinary kind may not show anything significant. In those rare instances in which an intelligence test may have been recorded before the injury there may be no evidence of impairment obtainable by such tests. Attempts have been made to construct special tests, directed to estimate, for example, the degree of abstraction of general qualities of which the patient is capable. For this purpose Goldstein has used a modification of the Kohs-Block test, and a modification of the Holmgren wool-test for colour blindness. Vigotsky's test is directed to the same object. As modified by Hanfmann and Kasanin it consists in asking the subject to classify a group of differently shaped, sized, and coloured blocks in several categories, each category having two specifications, e.g., tall and flat. The continuation of arithmetical progressions, for example, 1-1, 3-3, 5-5, has been used as a means of detecting if the patient can abstract a simple general rule.

Nichols and Hunt have devised some additional tests which have the merit of not requiring special apparatus. They have endeavoured to test the patient's ability to abstract a general principle ('find a system' as they call it) by dealing cards repeatedly in a certain order, and estimating how long it takes for the patient to hit upon the system of dealing that is employed. By playing draughts ('checkers') with him, they found that a patient with particular bilateral frontal lobectomy failed to improve at the game, i.e., to learn from experience, until verbally instructed. He could not abstract a general rule of play for himself. They also adapted the Knox-cube test, in which instruction in method again improved his performance, which without this was below average. The defects which these tests seemed to confirm in Nichols and Hunt's patient were, (1) lack of initiative or failure to construct hypotheses, i.e., to abstract from the concrete problem; (2) rigidity, or stereotypy of effort (there was no 'persistence with varied effort' except of the random kind); (3) confusion or inability to keep alternative modes of attack on problems isolated from one another, and (4) lack of integrative capacity—classification according to more than one category on, for example, height and shape, was not possible.

It is claimed that patients with brain injury, at least in certain areas, give a characteristic set of responses with the Rorschach test (Harrower-Erickson).

WAR NEUROSES

As was to be expected, no differences have appeared in the symptomatology from those observed in the last war. But the total incidence so far has been comparatively small, since for the vast majority of the combatants the exposure to stress has been much less continuous and very much less prolonged than in the war of 1914-18. There has been a preponderance of cases in which exhaustion has been a major factor, as in the Dunkirk evacuation following continuous retreat.

Unfortunately, in spite of all the attempts of medical authorities to warn Government departments of the need for a medical recruiting examination that would be a satisfactory minimum on the mental as well as the physical side, a considerable number of mentally unfit people have been passed into the Services. The most obvious requirement is the exclusion of the high-grade defectives who were recruited in such numbers last time and who usually became soon a burden on their fellows, but, no systematic attempt having been made to eliminate them, they have again been admitted in appreciable numbers. The haste with which recruiting medical examinations have had to be conducted in some quarters no doubt accounts for some of this, and also for the admission of types usually more difficult to detect, especially the psychopathic and the psychoneurotic. As the war proceeds these will gradually either be discharged, or find their appropriate and limited place within the Services, but much time and effort will have been wasted from neglect of old lessons.

Hysterical reactions of a gross kind have not been common, and have probably been more frequent among recently-joined recruits, intellectually or temperamentally defective, than among those who have been in action with the enemy. These hysterical reactions have occurred mostly in young psychopaths who have never done satisfactory work in civil life, in defectives, or in middle-aged reservists who disliked leaving their families and their comfortable jobs to return to Service life usually on a considerably less income, and with less comfort than they had in civil life.

Among members of the psychopathic group who have reported sick those of a solitary schizoid habit have been prominent. Barrack life has proved a bugbear to them. Another relatively numerous group among the young

recruits is that comprising the unstable psychopaths whose instability has shown itself principally in a failure to persist in any job for any length of time. The omission to take a reasonably complete history, often from lack of time, on the part of the recruiting doctor has led to the enlistment of some who have had a long history of psychoneurotic symptoms, or even of previous psychogenic breakdown.

Among the fatigued troops who returned from France, the commonest psychogenic symptoms were of the psychoneurotic-anxiety type; hysterical symptoms were rarer. A few cases presented a resemblance to a Parkinsonian picture--with relatively immobile facies, and a coarse tremor, in one case a typical pill-rolling tremor differing from the latter only in that it could not be controlled voluntarily for a short time (Sargant and Slater).

Amnesia for distressing experiences has not been as common as might have been expected from the literature of the last war. Most remember the terrifying episodes with complete detail. It is not to be expected that the recovery of the forgotten events by hypnosis or allied means will have the effect of producing more than a symptomatic cure; it is doubtful whether a man who has met a war experience by developing hysterical amnesia will face combat successfully in the future.

Most of such cases have recovered, as far as their symptoms are concerned, with mere rest and diversion. Discussion of their experiences in a frank manner helps to desensitize them. Hysterical amnesia should be tackled by persuasion, hypnosis, or narcosis, e.g., by hexobarbitone (evipan) or sodium amytal, in that order, if the method first tried is not successful.

Apart from the existence of recent unequivocal physical fatigue, rest in bed is bad, since this only encourages rumination. Diversion and occupation constitute the correct prescription. Any new appearance of symptoms must be promptly discouraged. An injudicious medical remark may perpetuate an otherwise transient symptom. For the more acute states of distress continuous narcosis has been used with apparently good effect in tiding the man over the period of more profound emotional disturbances.

Most of those who have displayed psychoneurotic symptoms have been predisposed, and the predisposition has usually been clearly evident in the previous history. They have either been timid people, by constitution or by upbringing, more usually the former, or they have had a considerable array of psychoneurotic or allied symptoms throughout their lives, or have been of psychopathic disposition.

One group has emerged among the administrative staff which did not receive much attention in the literature of the last war, namely, the mild depressions following a period of real overwork, usually in people of over-conscientious ('obsessional') disposition. Fatigue, partly self-induced by their habit of mind, has also been a factor in these cases, but it has been the fatigue of long office hours, rather than that of battle conditions.

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NERVOUS DISEASES

By J. PURDON MARTIN, M.D., F.R.C.P.

PHYSICIAN TO OUT-PATIENTS, NATIONAL HOSPITAL FOR NERVOUS DISEASES, QUEEN SQUARE, NEUROLOGIST, BRITISH POSTGRADUATE MEDICAL SCHOOL, LONDON

No survey of recent work in nervous diseases would be complete without reference to two works which, though not intended as original contributions, have enriched neurology during the period under review; namely, Denny-Brown's presentation of selected writings of Sir Charles Sherrington, and Kinnear Wilson's *Neurology*. The former brings home to a new generation of neurologists not only the work, but the method, of one who has done more than anyone except Hughlings Jackson to elucidate the functional organization of the nervous system. The latter is a textbook, admittedly left incomplete, on the scale of 'Oppenheim' and much after the same manner. The only British textbook with which it can be compared is Gowers' *Manual*, of which the second and last edition appeared in 1892; an equal life and influence may be hoped for Wilson's masterpiece.

It cannot be expected that every department of the subject should show noteworthy advances each year, and the new matter which is to be surveyed is not grouped exactly as in last year's presentation. Certain sections of the subject, e.g. that concerned with disorders of nutrition, are particularly active. On the other hand, much investigational work of all kinds in this country was interrupted by the war, and the knowledge of that published in Germany since the outbreak of hostilities has been cut off.

ANATOMY

In last year's survey reference was made to the recognition of dementia resulting from disease of the thalamus and it was suggested that the mental impairment resulted from the isolation of large areas of the cortex from thalamic influences.

A number of recent studies have brought more exact knowledge of the connexions of the thalamus.

Le Gros Clark and Dorothy Russell described a case in which hemiplegia acquired in childhood was associated with diffuse atrophy of the corresponding cerebral hemisphere and conspicuous atrophy of the optic thalamus. The condition of the hemisphere was such that it was practically equivalent to an experimental hemi-decortication. Atrophy of the thalamus was practically complete on the affected side with the exceptions of (1) the centre median nucleus; (2) the lateral geniculate body, and (3) a narrow subependymal zone of small cells. From this it was concluded that all other parts of the thalamus were concerned with the projection of impulses on to some part of the cerebral cortex. What seemed to be in many ways the complement of this case was provided by one investigated by Le Gros Clark and Ritchie Russell, in which symmetrical vascular lesions in the external capsules had nearly isolated on each side the cortex of the insula (of Reil) and of the upper surface of the superior temporal convolution in its middle third. The patient had cortical deafness. Examination of the thalamus showed complete cellular degeneration of (1) the centre median nucleus, (2) the medial geniculate body, and (3) the inter-geniculate nucleus. There was also partial cellular degeneration in the most ventral portion of the ventral nucleus.

and in the base of the pulvinar. The complete degeneration of the medial geniculate body was related to the cortical deafness. Le Gros Clark carried out experiments to see whether or not the degeneration of the centre median was associated with the isolation of the cortex of the insula; using monkeys, he produced destruction of the insular cortex by devascularization. The results, however, provided no evidence that the insula (of Reil) in the monkey received projection fibres from the centre median nucleus or from any other nuclear element of the thalamus. The connexions of the centre median remain undetermined.

Walker made a series of studies on the thalamus of the chimpanzee. From an examination of the retrograde cellular degeneration in the thalamic nuclei after large and small cortical lesions, the thalamic projection on the cortex was shown to be arranged as follows: (1) The large medial nucleus (*n. med. dors.*) sends its fibres exclusively to the pre-frontal region. (2) The anterior half of the lateral nuclear mass (*n. lat. vent.*) projects on to the motor and pre-motor areas, and (3) the posterior half of the ventral portion (*n. vent. post.*) sends its fibres exclusively to the post-central convolution. The projection of the lateral nuclear mass on the central gyri has a precise arrangement, the medial portions send their fibres to the inferior parts of the central convolutions, the dorsal portions send theirs to the superior parts, and the intermediate portions project on the middle parts. (4) The pulvinar projects on the posterior portions of the parietal and temporal lobes, the fibres from the lateral pulvinar nucleus going to the posterior part of the superior parietal lobule, those from the medial nucleus to the supramarginal gyrus, and those from the inferior nucleus to the temporo-occipital region.

Le Gros Clark and Northfield found that in the macaque monkey the main element of the pulvinar projected on to the posterior Sylvian area, behind the auditory area. The dorsal element, according to their findings, projected on to an area adjacent to the visual cortex.

PHYSIOLOGY

The hypothalamus

The American Association for Research in Nervous and Mental Diseases devoted its meeting in December, 1939, to discussion of the hypothalamus and the papers presented there, containing much new work, have been published in the association's annual volume. In this country during the past year a volume of lectures on the hypothalamus by Clark, Beattie, Riddoch, and Dott has been published, and abroad there has been a review by Ranson and Magoun in 1939.

The most outstanding developments of the last two years have been on functional localization in the hypothalamus, especially in relation to heat regulation and water metabolism. The most important recent work on heat regulation is that of Ranson and his pupils. They have found by local heating (by high-frequency currents passing between two implanted electrodes) that in cats the mechanisms of heat loss, especially panting, are activated when the temperature of the anterior hypothalamic area is raised. The active region lay in the mid-line immediately above the optic chiasma and in the pre-optic area. After the application of the heating current to this small area, panting began within 30 to 60 seconds, and was accompanied by sweating of the pads of the feet and by some vaso-dilatation. The rectal temperature always fell several degrees centigrade in conjunction with the panting and sweating.

The mechanisms of heat loss are primarily mediated by parasympathetic mechanisms, which include sweating and vaso-dilatation, coupled with the somatic reaction of panting. On the other hand, the mechanisms of heat

production—vaso-constriction and so forth—are mediated by sympathetic (adrenergic) mechanisms and the somatic reaction of shivering, and are activated by the posterior part of the hypothalamus (Keller *et al*). The function of regulating body temperature is thus a highly integrated reaction involving both divisions of the autonomic system as well as important somatic reactions.

Closely connected with the problem of heat regulation is the recent work of Uotila on the control of the thyroid by the hypothalamo-hypophyseal complex. Uotila found that the thyrotrophic hormone of the anterior pituitary, which is released when a rat is subjected to a cold atmosphere, failed to be released if the pituitary stalk had been previously sectioned without damage either to the anterior pituitary or to the hypothalamus. In a group of rats with stalks sectioned the thyroid failed to show the normal follicular hypertrophy in response to cold when the animals were placed for several days in a cold environment. The body temperatures of the animals gradually fell and the majority ultimately died when their temperatures were 15 to 20° C. below normal. Uotila's results suggest that there is a hypothalamic control over the production of the thyrotrophic hormone by the anterior pituitary.

Ranson, Fisher, and Ingram, and Gersh have studied the localization and mechanism of the control of water metabolism. It is now recognized that diabetes insipidus results from a deficiency of an antidiuretic substance which is essential for water conservation. This is evidently primarily controlled by cells of the median eminence at the root of the pituitary stalk and cells in the posterior lobe. When these cells are destroyed diabetes insipidus ensues. Moreover, when the supra-optic nucleus from which these cells receive a nerve supply is destroyed, the cells atrophy and diabetes insipidus ensues. If the posterior pituitary is destroyed, the cells in the median eminence and stalk may secrete sufficient antidiuretic substance to prevent the occurrence of diabetes insipidus. Ranson, Fisher, and Ingram consider that, in addition to being counteracted by the antidiuretic factor, the diuretic process is normally under the control of the anterior hypophysis and that the polyuria may therefore be regarded as resulting from an uncompensated activity of this part. Keller, Noble, and Hamilton found in 1936 that when diabetes insipidus had been induced in a dog by a lesion of the hypothalamus, it was abolished by subsequent removal of the pituitary, but that if anterior lobe extract was then administered subcutaneously the polyuria returned.

CLINICAL NEUROLOGY

Venous thrombosis in the central nervous system

Venous thrombosis in the central nervous system is now receiving a surprisingly tardy recognition. Consideration of the amount of research that has been devoted to other cerebral vascular disturbances and the number of far rarer diseases that have been carefully described, cannot but cause wonder that cerebral venous thrombosis has, till recently, attracted so little attention and that its clinical manifestations had not been recognized long ago.

The first group of cases to receive investigation was that in which aseptic thrombosis of a dural sinus occurred. The syndromes associated with septic thrombosis of the lateral sinus, and of the cavernous sinus were, of course, already well known. In 1931, Symonds gave a clinical description of cases of 'otitic hydrocephalus'. These, as the title indicates, were cases in which symptoms of hydrocephalus occurred after inflammatory conditions in the ears. In 1937, McAlpine recorded a number of cases of 'toxic hydrocephalus', in which similar symptoms followed infections of the throat or nose, and in

some instances recurred after subsequent infections. Later in the same year Symonds returned to the subject referring to post-mortem material and to two cases described respectively by Ellis and by Fraenkner, in which obstruction of the superior longitudinal sinus had been established during life and recovery had ensued. As in the previous instances, the symptoms in these cases were those of hydrocephalus, and they were subsequent on infective conditions in the ears, throat, and nose.

Further, in 1937, Onville Bailey and Hass reported some more complicated cases of thrombosis of the superior longitudinal sinus in infants in association with nutritional disturbances and with resulting mental deficiency. These were evidently cases of a much more severe type than those described by Symonds and by McAlpine. A point of interest is that their cases showed re-canalization of the sinus.

In a recent discussion (January, 1939) Sheehan and Martin described cases of a different type, namely, those in which, in the absence of any adjacent local disease, thrombosis occurred in a vein on the surface of the brain. In the first of Martin's cases the thrombosed vein had been seen at operation. The patient had suddenly been seized with convulsions ten days after a confinement, and having exhibited status epilepticus for more than 24 hours was left with hemiplegia, from which she eventually made an excellent recovery. Martin had seen three similar cases, following childbirth, all ending in good recovery. Sheehan, however, had seen several fatal cases in the pathological department of Glasgow Maternity Hospital. In these cases the convulsions had been followed by coma and death. At necropsy there was thrombosis in certain of the meningeal (superficial cerebral) veins entering the superior longitudinal sinus. This had produced an area of softening in part of the cerebral cortex, usually about 2 inches in diameter. The softening might involve the motor area and cause hemiplegia, but in many of the cases only the frontal or occipital lobe was affected. This condition, according to Sheehan, accounts for nearly all those cases diagnosed as 'late eclampsia'.

Though all these cases were consequent upon childbirth, there can be little doubt that cerebral venous thrombosis occurs in association with local infections in the same way as cranial venous sinus thrombosis. A number of the cases seen in children in which severe convulsions are followed by temporary or permanent hemiplegia are probably attributable to this cause. Symonds drew attention to them as complications of otitis media. Ferguson described a case of thrombophlebitis migrans in which convulsions and temporary palsies occurred, and it may be presumed that these were due to venous thrombosis in, or on the surface of, the brain.

Purdon Martin has seen several cases in which there was good reason to believe that paraplegia (partial or complete) was due to venous thrombosis in the spinal cord. In two instances the symptoms came on during the puerperium and one patient already had both femoral and cerebral thrombophlebitis.

It is evident that venous thrombosis affecting the central nervous system is by no means rare and may cause severe and possibly fatal symptoms. These symptoms are not, in themselves, very characteristic, but their sudden onset, in association with, or following, infection or childbirth indicates the probable presence of venous thrombosis.

The myeloscope

A glimpse into the future is afforded by the advent of the word 'myeloscope'. Pool devised an endoscope which is sufficiently small to be inserted into the spinal canal like an ordinary lumbar puncture needle, local anaesthesia being used for the skin and subcutaneous tissues.

The light-carrier of the instrument is approximately 1 mm in diameter. A small electric light bulb is attached to its spinal end where it projects 5.5 mm beyond the lip of the cannula. The bulb, however, does not necessarily project to that distance into the sub-arachnoid space. In the centre of the plug at the opposite end of the cannula is an aperture which receives the lens system.

Illustrations are given showing the views obtained with this instrument (Stern). The arachnoid membrane and dorsal roots can evidently be clearly inspected. Blood vessels are said to be easily recognized, the arteries and veins being distinguished by their difference in colour, as well as by the flow of blood which can be observed coursing in opposite directions in the two systems. The vessels in which these phenomena have been observed are those supplying the dorsal roots. It is said that they emanate from the spinal arteries and veins, but this is doubtful. The direction of arterial flow, observed in these studies, is caudad, the venous flow being cephalad. It is proposed to use this instrument as an aid in the diagnosis of diseases of the cauda equina and lumbo-sacral canal, and it is hoped eventually to apply the device to other portions of the spinal canal. The vertical extent of the theca visible appears to be approximately that corresponding to one spinal segment.

CLINICAL PATHOLOGY

Potassium in diseases of muscle

Following the observation of Allott (1935) that in familial periodic paralysis there was a marked lowering of the potassium content of the blood serum during an attack of this form of paralysis, considerable attention has been devoted to the investigation of the possible part played by potassium in various muscular diseases.

In familial periodic paralysis it was soon found that attacks of paralysis could be arrested by the oral administration of potassium chloride. The serum potassium does not rise in consequence of this administration as long as weakness is present, and so the potassium is probably absorbed by the muscles. During, and before, an attack there is a diminished excretion of potassium, the muscles possibly taking it up. When the low level of the blood potassium was first discovered, it was suggested that metabolic processes in the muscles might be inhibited as a consequence of lack of potassium in the serum for exchange, but it has been shown that in normal individuals a fall in serum potassium equal to that which accompanies an attack of periodic paralysis can be produced by the administration of adrenaline, but no muscular paralysis results. Low serum-potassium alone cannot, therefore, be the cause of the weakness.

In myasthenia gravis Cumings found an abnormally high content of potassium in the weak muscles, and that the administration of prostigmin, which restores the muscular power, causes a fall in the potassium content of the muscles and a rise of the potassium in the blood serum. There is not, however, any increase of potassium excreted in the urine. The potassium appears to be retained in the blood and to return to the muscles as the weakness of the muscles reappears.

In myotonia atrophica the myotonic muscles have a low potassium-content. Cumings found that after administration of prostigmin it increased to a normal level, but there was no accompanying change in the clinical functional state of the muscles.

The significance of these variations in potassium content in association with abnormalities of muscle function has not yet been determined, but the guess may be hazarded that they are concerned with disturbances of the

'buffering' mechanisms in the muscles. The variations in the amount of potassium may be less directly significant than changes in the manner in which it is combined with other substances—e.g. as diphosphate or monophosphate. In this connexion attention may be drawn to an element in the myasthenic disturbance of which sufficient notice has not been taken, namely, the failure of the myasthenic muscle to recover its store of energy at a normal rate or to a normal degree after fatigue.

Pudenz and his co-workers made some interesting observations in familial periodic paralysis. If the venous return from one arm is prevented, the injection of potassium chloride into an artery of the limb during an attack does not cause any return of function. Here there seems to be another indication, namely, that the manner in which the potassium is combined is all-important, and that other organs or tissues are probably concerned with its metabolism and responsible for presenting it in suitable form to the muscles. If, however, the circulation in one arm is completely cut off by a tourniquet, and potassium chloride is injected into the other arm, function recovers equally quickly in both upper limbs. If this observation is confirmed, it suggests the operation of a central factor which is independent of the circulation and, therefore, probably nervous.

There are many points of resemblance between the weakness of the muscles in an attack of periodic paralysis and that in myasthenia gravis, and the former has often been regarded as an attack of acute myasthenia. The findings described above seem to be in conformity with this view and thus to offer some confirmation of the similarity. An attack of periodic paralysis might be accounted for by the presence of a substance having an action opposite to that of prostigmin (or an acute deficiency of a prostigmin-like substance). This would have the effect of producing a weakness clinically comparable to that of myasthenia, associated with the passage of potassium from the blood serum into the muscles, and possibly other tissues. It may be supposed that the action of limited amounts of such a substance could in general be exhausted more rapidly by the provision of new supplies of potassium, and the failure of potassium chloride to terminate certain severe attacks would be accounted for by the continued presence of the disturbing factor. Laurent and Walther showed that large doses of potassium had a beneficial effect on the weakness in myasthenia gravis and that its use might enable the dose of prostigmin to be reduced.

NUTRITION

Wernicke's polioencephalitis haemorrhagica superior

Wernicke, assisted by an observation previously made by Gayet, first recognized the independence of this condition and described it in his *Lehrbuch der Gehirnkrankheiten* (1881). He considered that it was usually, but not always, due to chronic alcoholism. It was soon established that the condition was often a sequel to polyneuritis, but otherwise little further was learned of its aetiology until recently, when its relation to vitamin B deficiency began to be suspected.

The morbid change consists in minute haemorrhages which are usually limited to the region of the central grey matter around the third ventricle and cerebral aqueduct (of Sylvius), but may extend down into the floor of the fourth ventricle. According to Campbell and Biggart the corpora mamillaria are constantly involved. The clinical picture is characteristic: drowsiness, nystagmus, and ocular palsies leading perhaps to complete ophthalmoplegia. Weakness, tremor, and ataxy in the limbs may be noticeable. The disease runs an acute course and usually ends fatally in 8 to 14 days, and the patient

dies in coma. A slower course, ending in recovery, with residual mental disturbances, has occasionally been recorded.

Alexander, Pijoan, and Myerson produced Wernicke's disease in pigeons by depriving them of vitamin B₁ while adding ample supplies of other vitamins to their diet. Under such conditions the pigeons developed both 'beri-beri' and Wernicke's encephalopathy. If the pigeons were kept on an entirely vitamin-free diet the resulting beri-beri was only occasionally complicated by lesions of the Wernicke type. Wernicke's disease could not be produced in pigeons whose diet over a long period was deficient in all other vitamins, if the birds were receiving crystalline vitamin B₁ (aneurine).

The observations of Alexander and his co-workers not only indicate that Wernicke's disease is due to deficiency of vitamin B₁, they also suggest that vitamin B₁ in addition to its antineuritic properties possesses 'anti-angio-degenerative' properties and that more complete and longer deprivations are required to produce 'angio-degeneration' than to produce neuronal degeneration.

Effect of vitamin E deficiency on the nervous system

It has been known for some years that wheat-germ oil contained a substance designated vitamin E-- lack of which in the female caused abortion, and in the male testicular degeneration or sterility. There are probably several elements in the vitamin E group-- the α , β and γ tocopherols. The work of Einarson and Ringsted suggests that vitamin E, or at any rate one of its elements, is necessary for the normal nutrition of the central nervous system. Evans first observed that paralysis occurred in baby rats born of mothers fed on a diet deficient in vitamin E. This paralysis was not curable, but could be prevented by giving wheat-germ oil to the mothers. Einarson and Ringsted found that rats deprived of vitamin E became paralysed in their hind limbs. They first became markedly ataxic, then dragged their hind limbs along the floor, and later became completely unable to walk. The hind limbs and tail seemed to be anaesthetic, muscular atrophy set in and was occasionally extreme, and other trophic disturbances occurred.

The pathological changes were chiefly in the spinal cord, the posterior columns, anterior-horn cells, and in severe cases the pyramidal tracts all showing degeneration. The proximal parts of the posterior roots were also involved, and the anterior roots showed degeneration in keeping with that of the anterior-horn cells.

Favourable effects on amyotrophic lateral sclerosis and also on muscular dystrophy as a result of the administration of vitamin E or one of its components have been recorded by clinical observers, but it is as yet doubtful whether these observations can withstand criticism.

EXPERIMENTAL PATHOLOGY

The mechanism of concussion

An interesting piece of work and one which has immediate application to current problems is that by Scott entitled *The Physiology of concussion*.

Having devised an apparatus for recording in animals rapid changes in intracranial pressure, Scott found that in the dog at the time of a blow on the head, of sufficient force to cause unconsciousness, the intracranial pressure rose to a height considerably above the systolic blood-pressure. The intracranial pressure returned immediately to its normal level and remained there; the rise as recorded lasted between one-fifth and four-fifths of a second.

In another series of experiments the intracranial pressure was abruptly increased by injection of fluid into the cranial cavity and loss of consciousness

resulted as soon as the pressure was raised to a level above that of the arterial blood-pressure, although this pressure was maintained for only one second. At no time was consciousness lost in the dog when the intracranial pressure did not exceed the systolic blood-pressure, even though a high pressure below this level was maintained for long periods (thirty minutes).

After a blow on the head, there may or may not, according to Scott's findings, be a fall in arterial blood-pressure. Some of his animals showed a fall and this is in agreement with earlier findings by Cannon, but other of Scott's animals showed no fall.

Scott's findings lend strong support to the theory of concussion which ascribes the loss of consciousness to brief, but complete cerebral anaemia (Trotter, Cannon, and others). It is agreed, with Weiss and Baker, that the rate of circulatory change is important in the production of unconsciousness, but the question still remains whether or not anaemia for as short a period as one-fifth of a second is sufficient to cause it. If this theory, which has much to support it, be accepted, the cause of the rise of pressure at the time of the impact requires further discussion. It appears that Cannon offered the explanation that the skull was indented by the blow and its volume thus reduced. It is, however, more probable that in most cases deformation of the entire skull is a more potent cause than local indentation. Scott recalls that 'it is a well established geometric fact that any distortion of a sphere rapidly and materially reduces its volume.' The extension of that principle, which is equally well established by geometry, tells us that for a given surface area, the more nearly the shape approaches the spherical the greater is the contained volume. If this principle is applied to the human skull, it shows that compression in the direction of either of its short axes will reduce the cranial volume, but compression in the direction of its long axis must increase the volume. It is therefore to be expected that whereas a blow on the top or side of the head would cause sudden rise of intracranial pressure, a blow on the back of the head, or on the forehead, would cause a sudden severe reduction of intracranial pressure.

Scott's explanation is therefore not of general application. Sudden severe reduction of pressure may of course be an equally potent cause of unconsciousness, but that point has still to be determined experimentally. This need not be inconsistent with the 'anaemic' theory of concussion, for it is conceivable that the sudden severe fall of pressure between the skull and the brain, since it must cause great dilatation of the arteries, momentarily stops the flow of blood into the brain and, in fact, may cause sudden withdrawal of blood from it, both by veins and arteries.

THE MENTAL CHANGES RESULTING FROM COMPLETE OR PARTIAL AMPUTATION OF THE FRONTAL LOBES

It has long been recognized that lesions of the frontal lobes in the human subject gave rise to mental abnormalities, of which 'shallowness', lack of concentration, lack of persistence, and an abnormal tendency to joking were the most evident. In recent years, operative ablation of one frontal lobe has often been performed and in some cases it has been possible to make observations almost under the conditions of a laboratory experiment. The changes in many cases are somewhat elusive of analysis. Brickner made a remarkable study extending over eight years of a man who had bilateral frontal lobectomy and has brought this up to date in a recent paper. Jacobsen and his co-workers, Messimy, J. Fulton, and others have investigated the subject experimentally in chimpanzees and apes.

These animal experiments will be considered first. After removal of one frontal lobe no disturbance of behaviour or of response to intelligence tests

can be detected, but after removal of both frontal lobes various observers have reported striking restlessness and distractibility. Jacobsen *et al.* found that when tested by problems involving the retention and utilization of recent sensory experience, the operated animal failed; when, for example, food was placed under one of two cups which were then hidden for an interval by a screen, the operated animal was unable after four or five seconds to remember under which cup the food had been placed, whereas a normal chimpanzee could find the correct cup after intervals as long as five minutes. Moreover, an animal which developed neurotic symptoms when its discriminative powers were put to too great a strain, remained completely placid when put to the same test after removal of both frontal lobes.

In the human subject Penfield and Evans found that the maximal amputation of one frontal lobe alone produced little change in the patient's mentality, except some impairment of 'those processes necessary for planned initiative'. Rylander has published a psychological study of 32 patients on whom unilateral frontal lobectomy had been performed. Changes in volitional and psychomotor activity occurred in 22 cases: 14 showed restlessness, and 12 diminution of initiative and interest. Intellectual changes occurred in 21 cases. The most automatic forms of intelligence remained relatively well preserved. Attention, memory, and the ability to grasp the more common situations were not disturbed to any considerable extent, but the more complicated intellectual processes—higher forms of reasoning, thinking in symbols, judgment—had deteriorated. Emotional changes occurred in 30 cases. These consisted of a diminished inhibition of affective responses in 25 cases, and a displacement of the habitual feeling level in 28 cases—in 20 towards euphoria and in 8 towards depression.

Brickner's is so far the only study of bilateral frontal lobectomy in the human subject. His patient was a 40-year-old stockbroker who had a bilateral frontal lobectomy carried as far back as the premotor region. He was strikingly euphoric and his behaviour was puerile; 'Witzelsucht' was conspicuous and there was constant clowning and punning. The patient showed a gross lack of insight into his own condition. He was readily distracted, selfish, tactless, inconsiderate, and often rude. He also showed a lack of initiative and while expressing an ardent wish to return to work as a stockbroker, he made no move to put it into execution. With all these defects, his intelligence quotient, according to a series of tests, varied between eighty and ninety-nine, according to his co-operation and ability to concentrate at different times. Brickner considers that the fundamental defect resides in the patient's power of mental syntheses, that is, in the assembly of groups of percepts into groups of a higher order.

There is a group of head injury cases in which the patients are euphoric, easily distracted, and have little insight. Martini pointed out that these patients do not complain of the headache and other common after-effects of head injury—dizziness, nervousness, inability to concentrate—which are usual in those who, though depressed, have more normal insight.

Moniz devised and introduced the operation of 'pre-frontal lobotomy' as a therapeutic measure in chronic depressive psychosis, and Freeman and Watts recently described the results of this treatment in 48 cases. The operation consists of making an incision through the white matter of each frontal lobe in the plane of the coronal suture and the sphenoidal ridge; the cortex of the hemisphere is not divided except at the point on the lateral surface of the frontal lobe where the instrument is inserted and on the orbital surface, when the knife is carried down as far as the floor of the anterior fossa. Freeman and Watts state that the effect of this operation is to make the patient much less concerned with himself—'the displacement

of the affect from the self to the exterior. Patients note that they are gay or sad, startled or sarcastic, but particularly in response to external happenings. No longer do they respond unpleasantly to their thoughts; worries no longer obsess them; the visceral activities about which they complained so clamorously no longer possess an interest for these patients. They have lost their awareness of self to a greater or lesser degree. . . . The patient no longer compares himself with other people to his own disparagement

Whatever be the results of such an operation on depressive states, the procedure cannot represent more than a passing phase in the treatment of such conditions. Depressive conditions are essentially disturbances of function and will eventually be amenable to medical treatment. Operative treatment involves some mutilation of the mentality and a sacrifice of some of its highest qualities, which is repugnant to the human mind.

Lobectomy has, for the present, a legitimate sphere in the treatment of frontal gliomas, pending the discovery of some non-surgical means of dealing with these growths, which, because of their infiltrating or diffuse nature, are essentially unsuitable for the surgeon's efforts.

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TROPICAL MEDICINE

By SIR LEONARD ROGERS, K.C.S.I., LL.D., M.D., F.R.C.P., F.R.C.S., F.R.S.
LATE PHYSICIAN, HOSPITAL FOR TROPICAL DISEASES, LONDON

The impoverishment of the world, especially of the Continent of Europe, resulting from the destruction brought about by the megalomaniac lust for power of the totalitarian states, combined with the poor food crops resulting from the war and the prolonged severe winter of 1939-40, strongly predispose to the spread over central Europe from the east of epidemics of malaria, typhus, and relapsing or famine fever on even a larger scale than after the war of 1914-18. There was a good example of this after the Russian revolution, for in 1921 alone epidemic malaria, intensified by famine conditions, was estimated to have caused ten million cases, and as late as 1931 ninety per cent of the population of important areas of Russia were reported to be suffering from malaria. That prolonged war was also followed by disastrous epidemics of typhus and relapsing fever in eastern Europe with greater loss of life than that caused by the fighting. The present state of our knowledge regarding the prevention and treatment of these diseases which also prevail in many warm climates is therefore worthy of review.

MALARIA AND THE WAR

An illuminating account of malarial prevalence and prophylaxis during the previous world war has been furnished by the presidential address of Sir Rickard Christophers before the Royal Society of Tropical Medicine and Hygiene and the ensuing discussion. For example, the neglect of canals and drainage systems in parts of north Germany converted sporadic into epidemic malaria, and this makes it probable that the flooding of central Holland by saline waters, very favourable to the prevalence of the important Dutch carrier *Anopheles maculipennis atroparvus* (as pointed out on p. 143 of the 1939 Critical Survey on Tropical Medicine), is ominous. Again, in the last war malaria, with frequent relapses in men invalided home, proved a most serious handicap to our arms in the Balkans in spite of elaborate precautions, and the same was true regarding operations in Palestine, Mesopotamia, and East Africa. We must therefore consider how far we are better prepared than formerly to meet this menace.

During the stationary period in Palestine the use of antilarval methods, mosquito nets, and quinine prophylaxis was of considerable value in keeping down the incidence of malaria among our troops, but during the rapid advance to Syria they proved impracticable, and malarial fevers became rife. With the more rapid military movements of the present day the difficulties will be even greater. Drug prophylaxis will therefore be more important, and here the chemotherapeutic discoveries of the last two decades or so will be of some assistance. In the first place it is now fully established, through artificial malarial infections for the treatment of some nervous diseases, that quinine acts as a true prophylactic only against the direct injection of human malarial blood into susceptible subjects, and not against the natural mosquito-borne infection, owing to its failure to destroy the sporozoites. On the other hand, the prolonged prophylactic use of quinine does prevent, for long periods, the development of crippling clinical malaria, although fever eventually appears on the omission of the drug. Thus, prophylactic quinine will keep many men fit for duty under conditions in which its omission would be

followed by very numerous cases of incapacitating malaria. In Macedonia more efficient quinine prophylaxis resulted in the French troops suffering less from malaria than the British men in the same area.

More recently the discovery of atabrin, plasmoquine, and possibly some newer antimalarial drugs, has improved matters to some extent. Early statements that atabrin treatment was followed by far fewer relapses than reliance on quinine have not been fully confirmed, but the use of small doses of plasmoquine for a few days after an acute febrile attack has been cut short by one of those drugs, has been followed in India and elsewhere by a great reduction in the number of febrile relapses and earlier restoration of the efficiency of the patients. Thus, both in Panama and in Malaya prophylaxis by quinine or atabrin, followed by plasmoquine, has been reported to have almost abolished clinical malaria. Moreover, Sinton recorded experiments indicating that prosectasine is a true prophylactic against even the sporozoite stage of the dangerous *Plasmodium falciparum* infections. On the other hand, the sulphonamide group of drugs has proved less effective and more dangerous than the older antimalarial drugs. An arsenical benzene compound, mapharside (known as mapharsen in U.S.A.), has also been reported to be followed by fewer relapses than atabrin, but more experience is necessary to establish the superiority of these and other new drugs now under trial. It is fortunate that the large Dutch East Indian quinine supplies are open to the protectors of liberty, and the recent increased attention in this country to chemotherapeutic researches should ensure the needed supplies of anti-malarial and other such preparations. Atabrin and plasmoquine were formerly imported from Germany. The chemicals are now manufactured in Britain and are known by the new pharmacopoeial titles of Mephacrine hydrochloride and Pamaquin respectively.

Another danger is the distribution of dangerous anopheline carriers of malaria to new areas or countries. An outbreak of malaria in the previously free Barbados by this means fortunately was controlled, but more recently the introduction by sea of the dangerous African carrier, *A. gambiae*, into South America resulted in epidemic malaria spreading over a large part of Brazil.

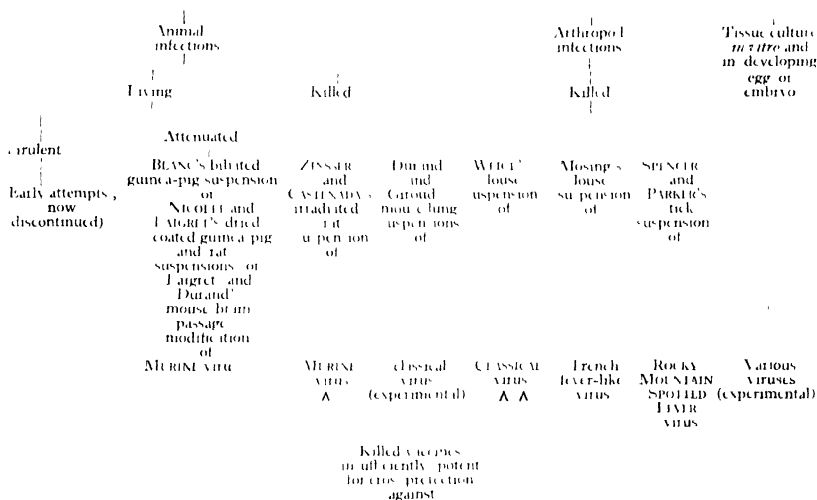
TYPHUS FEVERS

The world-wide distribution of the typhus group of fevers, due to the rickettsia group of organisms, is well shown in the map opposite p. 326 of Volume XII of the British Encyclopaedia of Medical Practice. On the following page will be found a table giving the principal features of the epidemic louse-borne form of temperate climates and the sporadic murine-, flea-, mite-, and tick-borne types of warm climates. The epidemic louse-borne typhus is always present in eastern Europe and often becomes epidemic in Russia and Poland in the winter months, and its prevalence is likely to be greatly favoured by the war impoverishment, the movement of armies, and the shortage of food. There is thus grave danger of the spread of epidemic typhus during the winter of 1940-41 over eastern and central Europe.

Unfortunately, no effective treatment of the disease is known, and the preventive de-lousing of large populations may well prove impossible under the prevailing conditions. The work of recent years on preventive inoculation against typhus fever is therefore of the utmost importance. As a considerable degree of cross immunity occurs between murine and louse-borne typhus, which has formed the basis of prophylactic methods of inoculation, the question must be considered on a wide basis. The accompanying table from a paper by F. Murgatroyd summarizes the present knowledge of rickettsial vaccines.

The essential fact governing the various attempts to immunize against typhus fevers is that killed vaccines have a limited protective value, virulent live vaccines cannot safely be used, and attenuated ones are not free from the danger of producing some severe reactions. Moreover, the cultivation of the organisms in sufficient amounts to furnish the quantities of killed vaccines required for large scale inoculation presents great difficulties, although some progress has recently been made in this respect. Weigl's original method (see Vol. XII, p. 335) of cultivating the rickettsial bodies by inoculation of them into the rectum of lice by means of capillary tubes necessitated the employment of a highly-skilled staff and several thousand

TABLE
OUTLINING RICKETTSIAL VACCINES



lice to produce 2,000 doses, so it is hardly possible to control a wide-spread epidemic by this means. An important advance has therefore been made by more recent methods of cultivating the organisms in minced guinea-pig tunica placed in serum-Tyrodé solution, which has enabled both the epidemic and murine strains to be maintained without loss of virulence for three or four years and formalized vaccines to be prepared. Zinsser and his co-workers have cultivated the Rocky Mountain fever and the Japanese mite-borne organisms by similar methods, so vaccines can be prepared against different forms of typhus fever. Another advance is the use of the chorio-allantoic membrane of the developing chick embryo for obtaining larger quantities of vaccine; and in 1937 to 1940 still larger concentrations of the organisms have been obtained by several workers from the lungs of rats and mice infected intranasally, which can be used for the preparation of dead vaccines.

The use of attenuated vaccines is illustrated by the work of Blanc, who used flea-borne murine organisms treated with ox-bile (see Vol. XII, p. 335), a thousand doses of which could be obtained from one guinea-pig. This vaccine has been used on a large scale in Algeria for the protection of the

indigenous population with good results, but in European subjects more severe and occasionally dangerous reactions were met with. It is important to note that, owing to cross immunity between the murine and the classical epidemic louse-borne typhus, murine vaccines so prepared can be used against the epidemic disease, and village epidemics of typhus have been brought to an abrupt end in this way. Moreover, Nicolle and Laugret attenuated the murine vaccine by drying and then retarding its absorption by coating with egg yolk and oil, and used it with success as a vaccine with the production of only inapparent infections in most subjects and without serious infections except in a few Europeans. Immunity lasting for from one to five years has been reported by the use of such attenuated vaccines. A mouse brain passaged murine vaccine was found to be even more successful and harmless. It has also been suggested that the difficulties in safely immunizing Europeans might be overcome by first producing a limited immunity by large doses of killed vaccines preparatory to inducing more complete and lasting protection by an attenuated one. In wide-spread epidemics only experience can determine the value of these various methods of protective inoculation.

CHEMOTHERAPY IN PROTOZOAL INFECTIONS

Recent work at the Liverpool School of Tropical Medicine has opened up a promising line of treatment by the discovery of the trypanocidal powers of synthalin and allied compounds, for a dilution of 1 in 100 million sufficed to destroy human trypanosomes *in vitro*. A number of such compounds have now been investigated, they have proved effective not only in African human trypanosome infections (although not in those of the South American *T. cruzi*), but also in those of kala-azar and in *Babesia canis* of puppies. Warrington Yorke concluded from trials of these drugs in the field that this advance is very promising, and they should prove of especial value in the occasional cases of trypanosomiasis and of kala-azar that prove resistant respectively to the arsenical and antimony preparations in general use for those infections.

BACILLARY DYSENTERY

The bacillary form of dysentery is especially prevalent among aggregations of persons living under difficult or deficient sanitary conditions, such as in lunatic asylums and armies in the field. This disease took a heavy toll of our forces in the Gallipoli peninsula in the last war and will probably prove important in the present one; knowledge of the causation, prophylaxis, and treatment of bacillary dysentery is therefore of special interest.

The problem is complicated by the occurrence of a number of closely allied causal organisms with different antigenic properties necessitating the preparation and use of different sera and vaccines, regarding which some advances have recently been made. The classification of the dysentery group of bacilli, given in Vol. IV, page 322, has been modified to some extent through the prolonged researches of J. S. K. Boyd in India. The non-mannitol-fermenting *B. dysenteriae* Shiga and *B. dysenteriae* Schmidt, with their high pathogenicity and effective serum treatment when active sera are available, remain unchanged. In the case of the mannitol-fermenting group the *B. dysenteriae* Flexner types V, W, X, Y and Z of Andrewes and Inman have been reduced by Boyd to V, W, and Z, and he has added three new ones, namely 103, P119, and 88-Newcastle-Manchester, to this sub-group. All these possess the Flexner group antigen. A further sub-group, which it is proposed to call *B. dysenteriae* Boyd, has been added by that worker, namely types 170, P288, and 01. These do not possess Flexner group antigen,

although they give the biochemical reactions of the Flexner bacilli. The *B. dysenteriae* Sonne sub-group of the mannitol-fermenting bacilli remain unchanged.

From the point of view of diagnosis of chronic cases of bacillary dysentery, in which the causal bacilli can rarely be isolated from the stools, by the agglutination test, the position has become more complicated in the case of the mannitol-fermenting group by these alterations and additions: for three sera are now required respectively for the Sonne, the remaining Flexner, and for the new Boyd sub-groups. It also remains to be ascertained whether effective sera against infections by these three sub-groups can be prepared.

TICK-BITE FEVER

By JAMES GLAR, M B , Ch B , D P H (WWRand), D T M & H , Dipl. Bact. (Lond),
SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH, JOHANNESBURG

DEFINITION

Tick-bite fever, the variety of tick typhus occurring in southern Africa, is caused by rickettsiae, transmitted by ixodid ticks, and characterized by a primary sore often having a blackish necrotic centre, by regional lymphadenitis, and in most cases by intermittent or remittent fever lasting ten to fourteen days and by a maculo-papular rash which appears on the third to the fifth day of illness and when profuse typically involves the palms of the hands and the soles of the feet.

History

Tick-bite fever was the descriptive name given by Nuttall in 1911 to a febrile disease mentioned by G. A. Turner (1908) and described in detail independently by McNaught (1911) and Sant' Anna (1911). Pijper and his co-workers, in an extensive series of investigations, proved that it was one of the typhus group of fevers, being caused by rickettsiae and transmitted by ticks (Pijper and Dau). Mason and Alexander, investigating the relation of this disease to the other tick-borne rickettsial diseases, described, amongst other features, cross-immunity between tick-bite fever and *fièvre boutonneuse*, and first noted the striking and characteristic intranuclear infections in cells in egg cultures of the rickettsiae.

ÆTIOLOGY

Geographical distribution

Tick-bite fever is wide-spread in southern Africa, cases occurring in every part of the country, but it is especially common in the bushveld areas of the Transvaal and along the coastal belt of Natal and the Cape Province. Cases are common in Southern Rhodesia and have recently been discovered in Northern Rhodesia. A similar disease has been described in Kenya (Roberts) and in Uganda (Loewenthal). In the towns and cities of South Africa infections are very rare in the fully built-up areas but are commonly contracted in the suburbs, especially in the better class suburbs where dogs are often kept as pets (Gear and Bevan, Gear and Douthwaite).

Incidence

The majority of reported cases have been in Europeans but natives are also susceptible, for recently cases occurring in native students were reported (Macvicar), an observation showing that the Bantus do not have any inherent immunity.

Most cases occur in adolescents and young adults, probably because persons of this age group are more enthusiastic in camping and shooting in the rural areas where ticks are numerous and the disease is endemic. All ages, however, are susceptible and cases occur in very young infants as well as in old age. In infections contracted in the suburban areas there is not any special age incidence.

The parasites

The rickettsiae causing tick-bite fever as seen in the scrotal exudate of infected guinea-pigs occur as bacillary, diplobacillary, and lanceolate diplococcal forms scattered in the cytoplasm of mononuclear cells, a distribution similar to that observed in Rocky Mountain spotted fever and *fièvre boutonneuse* and contrasting with the closely packed aggregations observed in the serosal cells of the exudate of guinea-pigs infected with murine and epidemic typhus (Gear, 1938).

In tissue culture and in cultures on the chorio-allantoic membrane of the developing chick embryo the rickettsiae may be located within the nucleus. This intranuclear infection is similar to that observed in Rocky Mountain spotted fever and in *fièvre boutonneuse*, and so appears to be characteristic of the tick typhus group (Gear, 1938, Alexander and Mason).

Reservoir host

An animal host has not been discovered, though it has been surmised that wild rodents may be reservoirs of the infection. Mason and Alexander reported the isolation of a virus immunologically identical with that causing tick-bite fever from a sick dog, but they concluded that this was probably fortuitous and that the part played by the dog was that of a conveyor of the infected ticks to man rather than a reservoir of infection. Rickettsiae morphologically and immunologically identical with those causing tick-bite fever have been isolated from ticks removed from dogs (Gear and Douthwaite) and from ticks removed from hares (Mason and Alexander) and also from cattle. As it has been shown in one species (Gear and De Meillon, 1940) that the infection is hereditarily transmitted from one generation of tick to the next, apparently indefinitely, no mammalian reservoir is necessary for preserving the infection.

Vectors

It seems probable that most species of ixodid ticks are capable of transmitting the disease. The following species have been stated to be vectors of tick-bite fever: *Amblyomma hebraeum*, *Rhipicephalus appendiculatus*, and *Boophilus decoloratus* (Pijper and Crocker), the common dog-tick *Haemaphysalis leachi* has also been proved to be a vector (Gear and Douthwaite; Gear and de Meillon, 1939). All stages of this tick—larva, nymph, and adult—are infective and there is hereditary transmission of the infection through the egg to the succeeding generations (Gear and de Meillon, 1940). It seems probable that hereditary infection also occurs in the other species of ixodid ticks. Amongst the factors which determine the importance of any species of tick as a vector are its opportunities for contact with and its readiness to bite man. Tick-bite fever is not more common in the suburbs of large towns, because the adult *Haemaphysalis leachi* does not seem to bite man readily. Only those who come into intimate association with dogs, while de-ticking them and crushing the ticks, or who allow tick-infested dogs to sleep on their beds or in their bedrooms, are liable to be infected by this tick. Most cases of tick-bite fever contracted in the rural districts are infected by larvae, probably because they are so small that they escape notice while biting and feeding. Nymphs and adults are usually detected and removed before becoming attached.

PATHOLOGY

As tick-bite fever is rarely fatal there have been few opportunities of studying the morbid changes in man, and no account of these is on record.

The disease in guinea-pigs

Tick-bite fever in guinea-pigs is much milder than either epidemic typhus or murine typhus, and of the animals inoculated only about 75 per cent show the characteristic febrile reaction. After an incubation period of three to seven days the temperature rises rapidly to attain a maximum of about 105° F. on the second day of fever, thereafter falling equally rapidly to normal, as a rule on the fifth day of illness. In adult male guinea-pigs the majority of reacting animals develop a scrotal reaction which, although well marked, is not as severe as that observed in guinea-pigs infected with murine typhus. In guinea-pigs inoculated with the virus intraperitoneally and killed during the fever the apparent lesions are enlargement and congestion of the inguinal glands which may show focal haemorrhages, fibrinous exudate on the tunica vaginalis and on the surface of the spleen, congestion of and often petechial haemorrhages in the tunica vaginalis and peritoneum, and congestion of and enlargement of the spleen and adrenals often with petechial haemorrhages on the surface. Small focal haemorrhagic areas are common in the lungs.

Microscopically sections of the tunica vaginalis and of the lungs show scattered inflammatory nodules consisting of infiltrating round cells, macrophages, and a few eosinophils, usually in relation to a small blood vessel which may be thrombosed. Sections of the brain disclose a few scattered nodules composed of an infiltration of round and mononuclear cells mainly in relation to small blood vessels. In sections stained by Giemsa's method rickettsiae may be detected in the cells of the nodules.

Immunological reaction

Guinea-pigs that have recovered from tick-bite fever and then been tested for immunity after an interval of about one month are immune to further infection with tick-bite fever but are susceptible to infection with the rickettsiae of epidemic typhus and of endemic murine typhus. On the other hand, a small proportion only of guinea-pigs which have recovered from either epidemic or murine typhus are susceptible to infection with tick-bite fever, so that in some cases complete protection and in others partial protection against tick-bite fever is conferred by a previous infection of epidemic or murine typhus.

CLINICAL PICTURE

Primary lesion

Man is infected by the bite of an infected tick, or by the introduction of the causal rickettsiae through an abraded skin, possibly through the intact skin. The infection may also be introduced through the conjunctiva by spurts of blood from crushed ticks, or by rubbing the eye with fingers contaminated while de-ticking domestic animals, especially dogs (Gear, 1939). At the site of the infective bite a characteristic local lesion usually develops. This primary sore, when first noticed, is a raised red papule, later developing into a painless ulcer with a black necrotic centre and a surrounding slightly raised erythematous areola. When the necrotic centre separates, a red non-suppurating floor is revealed. The primary lesion may be anywhere on the surface of the body, but is most commonly on the lower extremities; it often occurs on the external genitals, especially the scrotum where its presence, because it is painless, may be overlooked by the patient. Sometimes it appears on the penis where it may be mistaken for the primary chancre of syphilis, a suspicion apparently confirmed by the later development of a rash. In young children and infants the primary lesion is most often in the scalp, where it may be difficult to find, but a clue to its presence is usually given by the tender enlarged occipital or posterior cervical lymphatic glands. If the

infection is introduced through the conjunctiva the affected eye becomes inflamed, there may be slight ulceration of the conjunctiva, and the conjunctival vessels become engorged and petechial haemorrhages may occur. There is usually considerable swelling and oedema of the lids causing the eye to close. The regional cervical lymphatic glands become enlarged and tender. In many cases, especially in very severe cases, no primary lesion or regional enlargement of the lymphatic glands can be detected. It seems possible that in these cases the infection is introduced directly into the blood stream by the bite of the infective tick. The primary lesion, or *tache noire*, is usually apparent three to four days after the infective bite and increases in

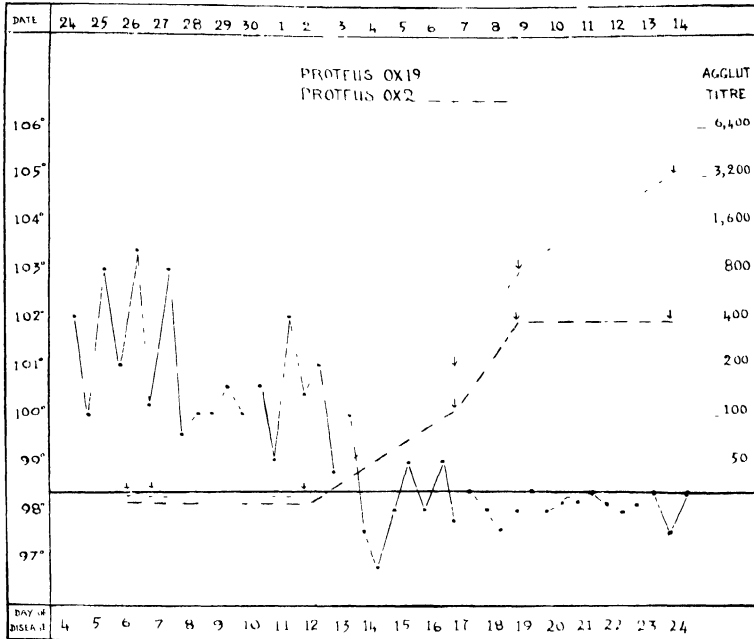


Fig. 6.—Temperature chart of a case of tick-bite fever, illustrating the development of agglutinins

size until about the seventh day, when the regional lymphatic glands become enlarged and very tender and general symptoms of illness appear.

The incubation period is usually exactly one week. A patient first feeling ill on Saturday or Sunday almost invariably states that he spent the previous week end on the veld. In other cases it has been noted that a week previously the patient had been de-ticking dogs.

The severity of the illness varies greatly. In many cases general symptoms are absent, only a primary sore and regional lymphadenitis being found. In a typical moderately severe case, the first of the general symptoms is lassitude with undue fatigue most prominent in the evening. Feelings of chilliness and slight rigors may follow, and the patient becomes feverish and complains of headache, which is worst in the evening and becomes so severe as to be often almost unbearable. At this stage there may be delirium which is most apparent during the night, and there may be visual or auditory

hallucinations. These symptoms are usually associated with insomnia. There is often slight deafness. Photophobia, associated with injected conjunctivae, is marked. The face is suffused and in severe cases the skin generally is congested and may have a dusky appearance most obvious on the face.

On the third to the fifth day of illness the characteristic rash begins to appear. The profuseness of the rash is directly related to the severity of the illness. In mild cases a few papules only may be detected. In very severe cases a profuse maculo-papular rash covers the whole body and characteristically involves the palms of the hands, the soles of the feet, and the face. In contrast to epidemic louse-borne typhus and murine typhus, the individual elements of this rash are relatively coarse, and the papules can easily be felt as shotty nodules in the skin. In severe cases large blotches or macules are also present, and in very severe cases petechial haemorrhages occur in the skin. The rash appears in crops, fresh papules being seen on each day for several days. The rash fades slowly during convalescence, taking several days to disappear completely.

Serious respiratory symptoms are rare, but a dry cough is frequent. Appetite is poor, and constipation is almost constant and may be difficult to relieve. The splenic area may be tender, but the spleen rarely becomes palpable. In children and young adults a general lymphadenitis with slight tenderness of the glands is common.

In mild and moderately severe cases the fever lasts ten days. It is intermittent or remittent, being much lower in the morning than in the evening, and terminates by gradual lysis. In severe cases the fever lasts up to fourteen days and tends to be more continuous than in the mild cases, but also terminates by lysis.

COURSE AND PROGNOSIS

In young adults and children recovery is rapid and usually there are no serious sequelae, but some patients complain of asthenia and mental depression for some weeks after defervescence. In older people complications are more frequent. As the disease primarily affects the vascular endothelium, most complications involve the circulatory system. The commonest is femoral thrombosis which occurs in a large proportion of cases in elderly patients. It occurs late in the course of the disease and is usually first noticed in convalescence. It may be further complicated by pulmonary embolism, sometimes fatally, the onset of which is marked by sudden acute pain in the chest followed by signs of consolidation of the lung. Femoral thrombosis is frequently followed by varicosity of the veins of the leg. Retinal haemorrhages may occur during the course of the disease and when coinciding with the appearance of the rash probably have the same pathological basis as the petechial spots in the skin (Gear, 1939).

The prognosis of tick-bite fever is good and even patients who appear desperately ill almost invariably recover. The mortality rate of all cases is about one per cent, death is usually caused by cardiac failure, pulmonary embolism, or broncho-pneumonia, occasionally it is directly caused by the severity of the toxæmia. Most fatal cases are elderly patients who, previous to the onset of the illness, had not been in robust health. In young healthy adults the mortality rate is nil.

DIAGNOSIS

The clinical picture of the disease, a primary lesion with a black eschar, regional lymphadenitis, a relatively coarse maculo-papular rash, involving the palms and soles of a patient complaining of severe headache, is so

characteristic that on clinical grounds alone there is little difficulty in the diagnosis.

Laboratory methods

The Weil-Felix test

The diagnosis can be confirmed by finding that the patient's serum, taken after the tenth day of illness, agglutinates one of the strains of *Proteus* used in the Weil-Felix test. Sera of cases of tick-bite fever agglutinate *Proteus* OX 19 and *Proteus* OX 2 and irregularly *Proteus* OX K. These agglutinins are only demonstrable after the tenth day of illness, i.e. convalescence. The titres of agglutination, although sometimes high, are low compared with the titres shown by cases of louse typhus. The reaction is therefore a group agglutination in the sense of Felix in his serological classification of the typhus group of fevers. On the average, over a series of cases *Proteus* OX 19 and *Proteus* OX 2 are agglutinated to approximately equal titre. *Proteus* OX K is irregularly agglutinated and rarely to high significant titres. There is, however, considerable variation between individual cases. Some show the presence of agglutinins to *Proteus* OX 19 only, some sera show high titre agglutinins for *Proteus* OX 19 and low titres for *Proteus* OX 2, many agglutinate *Proteus* OX 19 and *Proteus* OX 2 to approximately equal titre, and some agglutinate *Proteus* OX 2 only. This variability in serological reactions suggests the existence of different serological strains, but no other evidence favouring this hypothesis has been put forward. At present it seems more probable that one strain is capable of eliciting a different serological response in different individuals. Practically, a wide series of observations has indicated that cases showing agglutination of *Proteus* OX 2 only are almost certainly cases of tick-bite fever. Cases showing approximately equal agglutination of *Proteus* OX 2 and *Proteus* OX 19 are probably cases of tick-bite fever. On serological findings alone it is not possible to state whether a case showing agglutination of *Proteus* OX 19 to higher titre than *Proteus* OX 2 or of *Proteus* OX 19 alone is one of tick-bite fever, murine rat-flea typhus or louse epidemic typhus. However, a delay in the appearance of these agglutinins until after the tenth day of illness favours a diagnosis of tick-bite fever. The serological findings in tick-bite fever resemble in many respects those of the other diseases of the tick typhus group. In both Rocky Mountain spotted fever and in *fièvre boutonneuse* the late appearance of agglutinins for *Proteus* strains has been noted, and the approximately equal average titres for *Proteus* OX 19 and OX 2 described (Spencer and Maxcy, Felix).

Blood count

During the fever the red cell count may show an increase due probably to excessive sweating caused by antipyretic drugs and by the slight stagnation of the peripheral circulation. Early in the disease there is usually a leucopenia. In children and young adults this is often associated with a relative lymphocytosis. In middle-aged and elderly patients there may be no alteration in the percentage distribution of the leucocytes. Later in the course of a mild or moderately severe illness the leucocyte count tends to return to normal. In elderly patients and others who are severely ill, the initial leucopenia is followed by a neutrophil leucocytosis often as high as 15,000 per c.mm. and occasionally as high as 25,000.

Urine

Often a febrile albuminuria occurs. occasionally microscopic examination shows the presence of a few red blood cells. In some cases sugar has been detected during the fever, to disappear completely during convalescence.

TREATMENT

Prophylaxis

Tick-bite fever can be avoided by avoiding contact with ticks. Tick-infested dogs should not be allowed in houses and certainly not in bedrooms, or to sleep on their owners' beds or in babies' prams. When camping in or passing through tick-infested areas it is advisable to wear protective clothing. Soldiers in the field should not wear shorts, long trousers, with the lower ends bound down by anklets or puttees, are suitable. Each evening a careful search should be made for larval ticks, especially on the lower extremities and in the pubic region.

Protective vaccination

It is possible to grow the rickettsiae causing tick-bite fever on the chorio-allantoic membrane or the yolk sac of the developing chick embryo in sufficient numbers to make a vaccine, but the value of this vaccine has not yet been determined.

Specific and symptomatic

As yet no specific treatment of value for tick-bite fever has been discovered. In some cases one injection of neoarsphenamine (0.3-0.45 g. for an adult) if given early, seems to abort the attack, but considering the great variation in severity in different cases it is difficult to assess its value. In most cases no improvement is observed. Sulphanilamide and sulphapyridine and their related compounds are without effect.

The treatment is therefore mainly symptomatic, and the most important symptom requiring treatment is the severe headache. This may be difficult to relieve. The treatment given is aspirin, 5 gr. at 4-hour intervals, but it often requires more powerful analgesic drugs. Constipation is almost constant and in elderly patients may be difficult to overcome. In other patients it usually responds readily to the administration of salts (magnesium sulphate 1 oz. in the morning). Because of the danger of femoral thrombosis it is advisable to institute daily movement and elevation of the lower limbs. If femoral thrombosis has already occurred such exercise is dangerous until time for resolution of the clot has passed.

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VENEREAL DISEASES

By BRIGIET-COLONEL L. W. HARRISON, D.S.O., M.B. Ch.B., F.R.C.P. ED.
TECHNICAL ADVISER IN VENEREAL DISEASES, MINISTRY OF HEALTH, CONSULTANT
IN VENEREAL DISEASES, BRITISH POSTGRADUATE MEDICAL SCHOOL, LONDON

METHODS OF PREVENTION

According to Worms, no preventive ointment has yet given better results in experimental syphilis than the calomel cream originally recommended by Metchnikoff and Roux. It is rather surprising that the prophylactic properties of locally applied *meta*-amino-*para*-hydroxyphenylarsine oxide, commonly called arsenoxide and now sold under the name of mapharside which is believed to be the active derivative of arsphenamine compounds, have not been investigated more closely. The spirochaeticidal action of arsphenamine solutions *in vitro* is undoubted, and the good effects of local application of neoarsphenamine solution to the throat in Vincent's angina suggest that the arsenoxide might prove effective as a prophylactic agent, if applied locally. In the same connexion may be suggested investigation of the possibilities of locally applied sulphonamide compounds. Clinical experience in gonorrhoeal arthritis and in soft chancre has shown that a sulphonamide preparation may succeed if applied directly to the lesion, even though it has failed through the blood stream.

As regards the prevention of the spread of venereal diseases by treatment of the infected, in Great Britain since this war began two factors have operated in opposite directions. On the one hand, large movements of the population into rural areas many of which are out of the spheres of influence of civilian treatment centres, disturbance of the stability of family life, increased sexual activity resulting from war psychology, and so forth favour an increase of venereal diseases in the country. On the other hand, the drafting of a very large proportion of the young men into the armed forces where venereal infectivity is now controlled very effectively must drastically reduce the numbers of male carriers in the community and must therefore be a powerful factor in limiting the spread of these diseases, it may perhaps explain why at the time of writing, almost a year after the start of the war, there is no statistical evidence of any very great increase in the incidence of venereal diseases in Great Britain. With improvement in civilian control of the problem of the rural areas it may well happen that at the end of this war the position in respect of venereal diseases in this country will be better than it was at the end of 1918.

SYPHILIS

Bacteriology

The biological position of the organism of syphilis, its modes of reproduction, the question of its existence in a form other than the spiral which we know as *Spirochaeta pallida*, or as *Treponema pallidum*, and even its name have been discussed at great length since 1905 without any very satisfactory conclusion having been reached until fairly recently when the work of Séguin, of Manouélian, and of Simon and Molinédou has presented some clarifying

evidence. The chief of this is that by application of Séguin's modification of the Fontana-Tribondeau staining method it has been shown that *S. pallida* in its mode of reproduction is like other spirochaetes. That is, it divides transversely and may break up into fragments of two spirals, one, or even only half a spiral (spirochaetogenic granules), each fragment being distinguished histologically from debris or artifact by having adherent to it a short length of periplasm which retains somewhat the original spiral shape. The organism is said to be chiefly in this minute form in resolving and old lesions, and this explains why it is that, although a lymph gland may be infective for animals, the closest search may fail to reveal in it a typical *S. pallida*. Simon and Mollinédo have proposed that the demonstration of spirochaetogenic granules by Séguin's method should be employed as a routine diagnostic measure in the examination of gland juice in suspected cases, as in 15 cases they appear to have found typical spirochaetes in the gland juice of only 7 by the dark-ground method, and in 12 by the Séguin method, but spirochaetogenic granules in 14. They found also that, under treatment, spirochaetal forms disappeared quickly, but granules persisted much longer. The technique of Séguin's method, however, appears to be difficult to acquire, and it seems improbable that it will become popular for routine diagnosis.

Serum diagnosis

In the Survey on Venereal Diseases in Surveys and Abstracts for 1939, mention was made of the value of formal comparisons of the serodiagnostic methods of different laboratories, by means of tests of the same unknown sera, in raising technical standards. More evidence to the same effect has been provided by the U.S. Committee on Evaluation of Serodiagnostic Tests for Syphilis—a body composed of representatives of the U.S. Public Health Service and of the American Society of Clinical Pathologists—in its report on evaluation of the work of laboratories for 1938 and 1939; this report shows considerable improvement in the work of State laboratories as a result of these comparisons since they were first instituted. As evidence of the high standard of reliability to which serum tests for syphilis have been raised may be mentioned the fact that, in the four years during which these comparisons of serum tests have been going on in U.S.A., the five laboratories which have acted as standards for the Wassermann and the Eagle, Hinton, Kline, and Kahn flocculation tests respectively reported only four false positive reactions with the many hundreds of sera which they tested for the purposes of the enquiry. Similarly, in comparisons made under the auspices of the League of Nations, two methods of the Wassermann test and one flocculation, the Kahn, proved to be 100 per cent specific, and it may fairly be claimed that there is no more reliable laboratory procedure than a properly conducted serum test for syphilis. At the same time, as mentioned in the Survey for 1939, the comparisons held by the League of Nations and by the U.S. Committee have shown too clearly how very unreliable tests masquerading as Wassermann or as well-known flocculation tests can be in careless hands. This has a bearing on a tendency which has grown up within the past year or two to think that certain slide precipitation tests that have been invented may be carried out practically at the bedside. The tendency is dangerous, as modern research has done nothing to contradict but has strongly supported the resolution of the Second Laboratory Conference at Copenhagen in 1928 which emphasized 'the fact that, no less than the complement-fixation tests, these flocculation methods are, despite their apparent simplicity, extremely sensitive to the slightest differences in experimental conditions and subject to so many sources of error, in connexion both with

the execution of the test and the reading and interpretation of the results, that they must be placed only in the hands of specially trained serologists'.

In the same connexion may be quoted a resolution passed at the League of Nations Serum Conference in 1923 which ran 'From the experience obtained at this Conference that small differences in the technique may cause profound differences in results, it is of great importance, in regard to further comparative investigations, that the technique employed should be strictly in accordance with the directions of the authors of the methods. . . .'

If this resolution had been taken to heart and acted upon by all laboratories, the wide differences in results of tests of the same sera by what were stated to be the same methods in different laboratories collaborating in the U.S.A. comparisons, and seen to a less extent in the comparisons organized by the Ministry of Health in London, would not have occurred.

The demonstration by Gaetgens and others that an emulsion of cultural spirochaetes alleged to be *S. pallida* makes a more sensitive antigen in a syphilis complement-fixation test than does the usual cholesterolized extract of heart has led to work by Beck and by Eagle and colleagues which appears to show that the Wassermann reaction is a true antibody reaction against lipoids which are closely similar to those in *S. pallida*.

The new work opens up possibilities for improvement of the Wassermann test, and Richardson's method which is based on the principle of the reaction being a true antibody reaction is a distinct advance on the Harrison-Wyler in respect of both specificity and sensitivity. Erickson and Eagle foresee great possibilities for improvement in the development of *S. pallida* antigens.

In another direction diagnosis by agglutination of *S. pallida* seems to have been brought considerably nearer by the work of Tani, who has shown that, by treatment of rabbits' syphilomas with antiformin, an emulsion of real *S. pallida* can be formed which is agglutinable by syphilitic serum. Agglutination by syphilitic serum as demonstrated by this method ran rather closely parallel to the strength of their Wassermann reactions.

Treatment

Testimony to the efficacy of well-planned intermittent treatment has been afforded by Batchelor and Lees who, in correspondence over courses of treatment suggested for early syphilis in the armed forces, stated that in 675 cases of syphilis treated on those lines the relapses had been only 0.9 per cent.

In the Survey for 1939 evidence was advanced to the effect that a much smaller amount of treatment in the early stages of syphilis than is commonly prescribed confers a large amount of protection against late effects of syphilis. This was expanded in a paper on venereal diseases and life assurance read before the Assurance Medical Society early in 1940. As regards the treatment which had been given in the early stages to cases of syphilis which had eventually developed cardio-vascular syphilis, tabes, or general paresis, in 1,308 such cases reported on by seven groups of authors only 16 were classed as having been properly treated in the early stages of the infection.

In the same paper, besides the differences between males and females in respect of decreases and increases in mortality rates from general paresis, tabes, and aneurysm which were mentioned in this Survey for 1939, and were attributed to differences in the treatment received by the two sexes in the early stages of the infection, it was shown that, in the period 1921 to 1937, the mean age at death had changed as follows. General paresis, a rise in males from 46.5 to 51.0 years and in females from 47.8 to 50.3; tabes, a rise in males from 56.5 to 61.1 and in females from 57.8 to 59.8; and aneurysm, a rise in males from 55.7 to 59.5, but a fall in females from 62.2 to 59.3 years. It seems probable that here also the differences are attributable

to the fact that in the early stages the males were on the whole better treated than the females.

Ehrlich's goal of *therapia sterilisans magna* for syphilis may be approached by the five-day treatment which has now been under investigation by a special committee in New York for some years. On the strength of an observation by Hyman in 1931 that speed of administration is a very important factor in the provocation of toxic symptoms, Chargin, in collaboration with Hyman and Leifer, began to treat early syphilis by an intravenous drip method in which 0.1 g. of neoarsphenamine was administered hourly for 10 to 15 hours a day for 4 to 5 days, the total dose being 4 to 5 g. Of 86 cases treated by this method 7 disappeared and, counting them as failures, the method was considered to have been successful in 83 per cent of the cases. Toxic effects were generally mild, but rather frequent: they included one death from encephalitis, 35 per cent polyneuritis (10 per cent moderately severe), and dermatoses in more than half the cases. At the time of writing the authors had substituted mapharside for neoarsphenamine in the hope of reducing toxic effects. In this respect they had been so far successful in 300 cases without any loss in the therapeutic efficacy of the treatment. The authors and the committee are properly cautious in their assessment of ultimate results of this treatment which is clearly suitable only for hospital practice.

GONORRHOEA

Diagnosis

The tendency of sulphonamide treatment to suppress symptoms has stimulated investigation of cultural methods, and it is now becoming much more generally acknowledged than formerly that by culture an important proportion of gonococcus carriers are detected who would be missed if reliance were placed only on microscopical examination.

The discovery by culture of gonococcus carriers in women with no history or sign of gonorrhoea, as in the 10 found in the series of 500 unselected pregnant women examined by Tucker *et al.*, may lead to the greater use of this method as a matter of routine in gynaecological examinations.

Treatment

The fact that nearly 300 articles on the use of sulphonamide remedies in gonorrhoea were listed in Index Medicus for 1939 is good evidence of the great interest which this form of treatment has aroused. There is still much difference of opinion on the subject of dosage and the best time to start the treatment. As regards dosage there is a fair amount of evidence in both cultural and clinical work that the gonococcus can acquire a tolerance of these remedies. This indicates that the best plan of treatment is one which gives the attack every advantage possible from the outset, and that therefore the highest dosage which the patient can tolerate should be prescribed at once. Conversely, it means that a timid dosage from the start may result only in the development by the organism of complete resistance to chemotherapy. Two other factors also favour a scheme of high dosage and the shortest period of treatment compatible with eradication of the disease. One is the greater probability of the development of blood dyscrasias from long drawn out treatment than from short and sharp, relatively heavy dosage courses, the other is that, under a prolonged timid dosage scheme of treatment patients are more apt to discontinue treatment whilst still infectious than under a short and sharp scheme. A factor which favours success of sulphonamide therapy of gonorrhoea is an acquired resistance. Indeed, on the evidence which has so far accumulated it seems safe to say that all the sulphonamide compounds, except sulphapyridine, need the assistance of this

factor so much that, when using them, far more is gained than lost by waiting for its development. A disadvantage of waiting is the opportunity which it gives the gonococcus to invade the posterior urethra and adnexa, and therefore for the development of troublesome complications. Fortunately with sulphapyridine more seems to be gained than lost by starting its administration at once, and it is therefore the remedy of choice in all fresh infections. The dosage, as indicated, should be as high as possible, 4 g. or more a day for an adult male and 3 g. for a female, the patient being encouraged to put up with nausea as well as possible. I try to keep male cases on 4 g. a day for 7 days, and then stop if the discharge ceased about the third day, but others prefer to continue treatment for another week. The doses should be distributed evenly throughout the day. I try to administer 4 g. on the first day, even if the patient is seen in the late afternoon, and the first and last doses on the succeeding days are 1 g. (2 tablets). In cases in which it is possible for the patient to remain at home for a few days the intensive method of Bowie *et al.* mentioned in the Cumulative Supplement, Key No 576, should be seriously considered. The more intensive the methods developed, with corresponding shortening of the duration of treatment, the greater is going to be the effect on the incidence of the disease in the community.

Failures with a well-conducted sulphonamide treatment are now so few that, when they occur, the practitioner is apt to be at a loss what to do next. In such cases it pays well to search for a badly-draining focus, and there is also good evidence of the value in resistant cases of inducing fever by a suitable agent such as dmelcos or T A.B. vaccine.

Sulphonamide treatment sometimes fails in cases of arthritis, and here injection of the remedy into the joint as recommended by Cain *et al.* (see Cumulative Supplement, Key No 576) may be worth a trial.

In vulvovaginitis of girls the indication seems to be to use sulphonamide treatment to the best advantage, and to resort to local treatment, e.g. by theelin (oestrone) pessaries, only when treatment by mouth fails. Thus, induction of the masturbation habit, a great danger of local treatment, is avoided.

CHANCROID

In the article on chancroid in Volume III (1937) it was mentioned that, although this disease is commonly attributed to infection with Ducrey's bacillus, in fact a number of conditions due to other infections are usually diagnosed as chancroid. The reason is largely due to the difficulty of demonstrating *H. ducreyi* in the lesions, and the fact that even if an Ito-Reenstierna skin-test is made a positive reaction means only that the patient has at some time suffered from this infection. A more direct method of diagnosis being desirable, the new cultural method of Anderson and Snow is worth attention. The chorio-allantoic membrane of an 11-day old chick embryo is inoculated with a few drops of the pus from a bubo, and in the amniotic and allantoic fluids the organisms are easily demonstrable at the end of 48 hours.

Evidence of the value of sulphonamide treatment of chancroid has been strengthened by the reports of a number of workers, and it will undoubtedly be the first to be tried in future, perhaps in conjunction with such a vaccine as dmelcos. Attention is due also to an abortive treatment of bubo recommended by de Gregorio. In this, dmelcos is injected into the gland every three or four days starting with 0.5 c.cm. and increasing by 0.5 c.cm. The treatment is useless, however, after suppuration has begun.

GRANULOMA INGUINALE

Esthiomène is now usually attributed to the virus of lymphogranuloma inguinale, but Schoch and Alexander have described two cases of

elephantiasis and ulceration of the vulva which they regard as due to granuloma inguinale because the Frei reaction was negative and the response to antimonial (stibophen, foudin) treatment was good. In a male case of typical granuloma of the left groin also they saw elephantiasis of the left side of the penis and scrotum.

Greenblatt *et al.* have produced what they consider to be conclusive proof that granuloma inguinale is due to Donovan bodies, which they regard as protozoa. They have shown also that the swelling in the groin in these cases is not mainly glandular, but due to granulomatous reaction of the corium and subcutaneous tissues. For this reason they propose to call the lesion a pseudo-bubo. Although the groin lesion is not in the main a glandular one, these workers think that the organisms reach the groin by the lymphatics and, after setting up some reaction in the glands, they quickly invade the overlying subcutaneous tissues and skin.

LYMPHOPATHIA VENEREUM

As a confirmatory test of lymphopathia venereum Decker *et al.* recommend the intravenous injection of mouse-brain antigen. In cases of lymphopathia venereum infection, whether inguinal or genito-ano-rectal, the injection is followed in about 8 hours by a rise of temperature which may reach 103° or 104° F. within the next 12 hours. The optimal dose appears to be 0.1 c.c.m.

The fact that lymphopathia venereum is a general disease is testified by the skin allergy, the increased blood sedimentation rate, and other signs. Gsell has reported on blood and bone marrow changes similar to those found in multiple myeloma in a case of ano-rectal syndrome due to lymphopathia venereum infection. In a specimen of bone marrow obtained by sternal puncture there was a great increase in the number of plasma cells and of immature myelocytes, and polynuclear cells were much reduced.

In cases of lymphopathia venereum with open buboes which resist sulphonamide treatment it may be worth while to try the application of a filtrate of the contents of lymphogranuloma inguinale buboes, according to the method of Zahawi and Akrawi. The contents of a bubo are put into glucose broth and incubated for 3 to 5 days at 37° C. after which the mixture is filtered through a Seitz filter and the filtrate applied on gauze to the open bubo or injected into its edges. In the same connexion may be mentioned the injection of Frei antigen into the lymphopathia venereum buboes or into rectal lesions, according to the case, which is recommended by Caminopetros. The dose is 1 to 2 c.c.m. and in a bubo it excites a smart local and general reaction with fever. The injections are repeated every 3 or 4 days, and when the bubo softens it is aspirated, after this the process recedes rapidly. Injections into rectal, vaginal, and anal lesions did not provoke such strong local reactions as those into buboes, but the first four or five were followed by fever. The intravenous injection of Frei antigen has been reported on favourably by Kornblith as a result of an experience of 207 cases. The dose of the antigen, which was prepared according to Frei's original directions, was 0.3 c.c.m. and it was given three times a week. The first few injections usually produced a general febrile reaction, with corresponding general symptoms.

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TUBERCULOSIS

By S. ROODHOUSE GLOYNE, M.D., D.P.H.
PATHOLOGIST, LONDON CHEST HOSPITAL

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Recent advances in the study of tuberculosis have been made on the following lines

DIAGNOSIS

New tuberculin patch-test

For tuberculin diagnosis a patch test has lately been introduced which is considered useful for the investigation of large groups of persons in whom injections are laborious, and for small children. It consists in the application to the cleansed skin of a strip of filter paper previously saturated with undiluted old tuberculin, and dried. The moisture of the skin is believed to dissolve the tuberculin out of the paper sufficiently to produce a skin reaction. The patch is removed at the end of 48 hours, and the result is read 24 hours afterwards. Though the test has a value in cases in which an intracutaneous inoculation cannot be applied, it is probably not quite so reliable.

Miniature film radiograms

Chest radiology has been advanced by the development of the miniature film method, by means of which chest radiograms of large groups of persons can be obtained rapidly (Shanks, Sutton). The method consists in a photograph of the chest as it appears on the X-ray screen, and enlarging the photograph so obtained. By screening persons in quick succession, and using a special film, many persons, such as recruits, can be examined in a short space of time. The outfit, consisting of camera and enlarging unit and X-ray apparatus, is, however, expensive. This is to some extent set off by the fact that it can be used as a mobile unit. The method has been made practicable by the increase in brilliance of the screen image obtained in X-ray work, the development of high-speed lenses, and general improvements in photographic technique, especially as regards miniature films.

PROGNOSIS

Tuberculosis in relation to life assurance has received some consideration. Statistics confirm the clinical view that young underweight proposers, especially if they are tall, with a family history of one or more cases of pulmonary tuberculosis show an excessive mortality. With regard to other types of tuberculosis, Otto May, judging the question from the point of view of British assurance practice, considers that no case of genito-urinary tuberculosis should be accepted within five years of the disease, except with a maximal lien, but that a less grave view may be taken of tuberculous joints and bones, and tuberculous adenitis, and that a primary pleurisy, whether dry or with effusion, must for assurance purposes always be regarded as probably of tuberculous origin, and necessitate the imposition of some lien in every candidate with such a history, until at least seven years have elapsed, the amount of lien being a minimum of 20 per cent.

GROUP SURVEYS

Group investigation of persons who are specially liable to infection, such as medical students and nurses, continue to be reported. D'Arcy Hart,

Hilton, and Morland, at University College Hospital, London, show that of 417 medical students examined, important tuberculous lesions were found in 6.1 per cent of men, and 7.4 per cent of women during a three-year period of investigation. The reports published on nurses are still inadequate. Some deal with tuberculin tests only, others with X-ray examinations, and others again with morbidity and mortality figures. It would probably be safe to say that the majority of nurses have a positive tuberculin reaction by the time they finish training, but that during the period extending from the date of entry to a year after completion of training, the incidence of breakdowns from tuberculosis does not exceed 5 per cent.

TREATMENT

Sulphonamide compounds

The sulphonamide group of drugs has now been tested in the treatment of tuberculosis. Although a few series of encouraging results in experimental animals have been published, the results in man have been disappointing, and at the moment it does not look as though this group of drugs will afford much help to the tuberculosis physician.

Extra-pleural pneumolysis

On the surgical side the most recent advance has been the development of the operation of extra-pleural pneumolysis by means of which an upper lobe cavity, which cannot be dealt with by the separation of adhesions by endoscopy, may be collapsed without resorting to the more serious operation of removing the ribs by thoracoplasty. It is too early yet to assess the ultimate results.

Interruption of pregnancy

Medical conferences in various countries continue to discuss the question of the interruption of pregnancy in women in whom tuberculosis is active, but so far unanimity has not been reached. It is obvious that a woman with active tuberculosis and pregnancy has two risks to face instead of one, but recent investigations suggest that with a continuous sanatorium régime during the months of pregnancy and for some time afterwards, the risks are considerably less. The economic difficulties, however, are serious.

TUBERCULOSIS IN PRIMITIVE PEOPLES AND NON-IMMUNIZED RACES

Statistics on this point are still rather meagre. At one end of the scale are the figures of the war of 1914-1918, which show a mortality amongst the French Senegalese troops of 111.4 per 1,000, which is probably the highest so far recorded. On the British side, the mortality of Indian troops was 27.4 per 1,000 as against 1.1 per 1,000 amongst the British soldiers. At the other end of the scale, are figures of partially immunized races; thus in the United States, the negro mortality is 2.33 per 1,000 (three times that of the white population), amongst Indians of the Canadian Reservation, 5.46 per 1,000, and amongst the Maories of New Zealand, 4.2 per 1,000. The disease is predominantly of the pulmonary type, tending to the acute and subacute variety found in European children, and the recovery rate is small. Non-pulmonary tuberculosis is not common. Shortly before the present war, the League of Nations had commenced an inquiry into the whole subject in Asia. The numerous problems in the control of the disease centre round questions of immigration of infected persons, overcrowding due to increasing

trade and industrialization (e.g. in factories, ports, and mines), the recruiting of native armies, the prevalence of unhygienic native customs, and the cost of adequate preventive measures. Sanatorium treatment is generally impracticable amongst primitive peoples.

WAR AND TUBERCULOSIS

At the time of writing, the effect of the war on tuberculosis mortality is naturally causing some concern. During the last war, it was the experience, not only of the combatant nations, but of the neutrals, that the tuberculosis mortality rose under war conditions. Obviously the risks of infection are increased when groups of individuals live at close quarters in trenches, dug-outs, or below decks in ships, and malnutrition is an added factor in pre-disposition. The following graph shows the effect of the war of 1914-1918 on the populations of Europe.

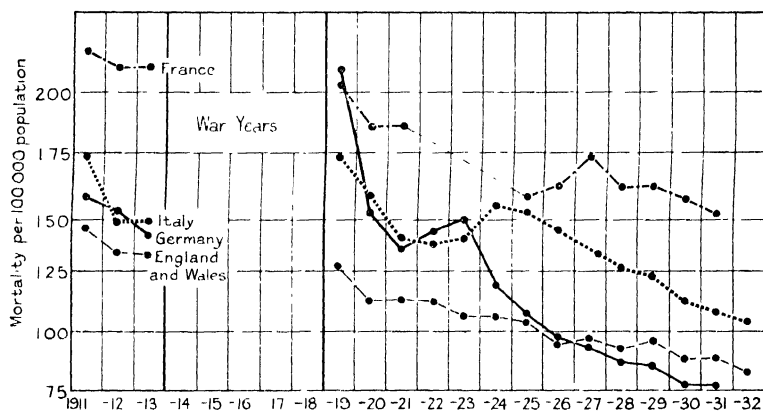


Fig. 7 - Mortality per 100,000 population from tuberculosis (all forms)
(From *Tubercle*, 1937)

The effect of trauma is difficult to determine. Tubercle bacilli are very unlikely to reach a wound directly from outside, though it is conceivable that they may very occasionally be carried to an injured area by the blood stream from an active focus elsewhere; or a quiescent tuberculous focus may be lighted up by the liberation of encapsulated living bacilli. Such contingencies are extremely difficult to verify afterwards, and the opportunities for doing so at the time of injury rarely exist. Acid-fast bacilli other than tubercle bacilli have been found in a wound exposed to sea water.

SOCIAL HYGIENE AND AFTER-CARE

The amount of public money available for the treatment and control of tuberculosis is likely to be strictly limited for some time to come. Heaf recently emphasized the following points, (1) Institutional care of the infective incurable case merely from the point of view of segregation is unnecessarily expensive under the present costly hospital or sanatorium régime; (2) a less expensive bed system with some remunerative employment during recuperative periods under medical supervision would meet such cases;

(3) the fully equipped sanatorium with operating theatre should be reserved for the curable patients and those requiring collapse therapy; (4) the industrial world has no place for weaklings; (5) schemes for re-absorbing ex-patients into industry are at present inadequate and a national scheme of rehabilitation is required.

BOVINE TUBERCULOSIS

Until recent years it was generally believed that the bovine strain of tubercle bacillus only rarely infected the lung. A. S. Griffith and his co-workers have now shown that bovine tuberculosis is commoner than was formerly believed. Up to 1922 only four cases had been recorded in Great Britain. Griffith has now collected 163. It is noted that more cases have been found in the north of England (1.6 per cent) than in the south (0.6 per cent), and a larger number still in Scotland, where the percentage of cases of pulmonary tuberculosis attributable to the bovine strain amongst those so far examined has ranged from 4.6 per cent in southern areas to 8.5 per cent in rural parts of north-east Scotland. In a review of the clinical evidence Griffith enumerates four possible methods of infection: (a) alimentary; (b) air-borne infection with the bovine bacillus from person to person; (c) rupture of a tuberculous bronchial gland containing bovine bacilli; and (d) direct transmission of bovine bacilli from cattle to persons handling them. This new aspect of 'cattle contacts' needs special emphasis in all persons employed on farms.

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RADIOGRAPHY AND RADIOTHERAPY

By RUSSELL J. REYNOLDS, C.B.I., M.B., B.S., F.R.C.P., D.M.R.I., F.F.R.
PHYSICIAN IN CHARGE, DEPARTMENT OF RADIOLOGY AND ELECTROTHERAPY, CHARING
CROSS HOSPITAL, LONDON, HONORARY ADVISER IN RADIOLOGY TO THE MINISTER
OF PENSIONS

The following is a short, critical survey of recent work in diagnostic and therapeutic radiology. Many of the techniques described have been in use for some time, but experience has proved their worth, and they have been, from time to time, modified and improved.

On the diagnostic side of radiography are discussed the following techniques which have been of sufficient importance to create special interest. Some of these are entirely new conceptions, whereas others are noteworthy improvements in existing methods: (1) cineradiography, (2) kymography, (3) tomography, (4) radiography of soft tissues, (5) radiography of joint cavities without the introduction of opaque media, (6) ventriculography and improvements in the existing technique of encephalography, (7) arteriography, (8) the Lysholm grid, (9) mass radiography.

Recent advances in the therapeutic branches of radiology include the following: (1) chronic mastitis, (2) the wide-field X-ray treatment, (3) the regional X-ray bath, (4) super high-voltage therapy (running between 400 and 1,000 kv), (5) Chaoul contact-therapy.

RADIOGRAPHY

Cineradiography

Ever since the discovery of X-rays by W. K. von Röntgen in November, 1895, radiologists have been attempting to reproduce photographically the moving shadows seen on the fluorescent screen. The principle of the ordinary cinematograph was established in 1896, and the manifest advantages of this, could it be combined with X-rays, were quickly apparent.

Methods of Production of Cinematographic Films

So far there would appear to be only three means by which an X-ray cinematographic effect can be obtained, namely, (i) *the synthetic method*, (ii) *the direct method*, in which a series of skiagrams is taken at short intervals upon a long strip of film, and (iii) *the indirect method*, in which a photograph is taken of the image appearing on a fluorescent screen.

The synthetic method

In 1897, John MacIntyre showed a film illustrating the movements of the bones of a frog's leg to the Glasgow Philosophical Society. The movement he showed was lifelike and informative, but the picture was, of course, synthetic. He had taken a number of ordinary isolated radiographs of the leg in different positions, and then, arranging them in order, had transferred them to a cinematograph film. This was an extraordinary feat, considering the primitive and feeble apparatus in use at the time, and testifies to MacIntyre's ingenuity and patience. A modification of the synthetic method

is still used by Van de Maele and some other workers; in this a series of isolated films is rapidly taken, the movement being carried on the whole time. This modification can hardly be compared to MacIntyre's original process, in which a film was taken, the object to be radiographed being held still as long as it was required, then, after one exposure, being moved to a fresh position ready for the next. When the series had finally been completed, there remained the problem of transferring it to a standard-sized film for projection. It was, moreover, quite useless for obtaining representations of involuntary movements, such as those of the alimentary canal, which could not be kept stationary while the exposure was made.

The direct method

The essential features of an apparatus for this technique are that there should be some method of passing a large area of film into position, holding it absolutely still while the exposure is made, and then carrying it through the various developing processes. These requirements are not easily fulfilled, and present many serious mechanical problems. In order, as far as possible, to minimize the difficulties of designing the apparatus, a restricted field of 4 by 5 inches is usually employed, but this sets a limit to the parts of the body which can be examined.

It is necessary, as in the synthetic method, to reproduce the serial skiagrams for projection purposes on a standard size (35 mm. or 16 mm.) cinematograph film. In this connexion it must be remembered that, if a smooth movement is to be obtained, the film must pass through the projector at a minimum speed of 12 frames per second.

The synthetic method naturally dropped out when it was found that it was possible to record movements in small fractions of a second. A. L. Barclay designed a camera for the production of cinematographic films by the direct method, and Van de Maele has brought this method to a high state of perfection.

In the direct method, the negative film obtained gives images of the same size as in ordinary radiography.

The indirect method

This method has been developed and apparatus has been designed for practical use in clinical diagnostic and experimental work by the author (1921-1934).

In this method, the negative is made in a cinematograph camera which obtains an image directly from the fluorescent screen; the film can then be used without reduction, either as a negative, or reproduced by contact as a positive. In the latest work by this method, short lengths of positive film are made, containing one or more cycles of movement, and these are joined into bands for continuous projection. In this way they can then be projected and studied at leisure.

Size of field

The standard size of field for normal work is 12 by 15 inches; this is large enough to allow the whole thorax to be included. The apparatus can, however, be adapted to take pictures of any dimensions smaller than this, with consequent increase in detail. In this way any single joint may be made to cover the whole field. The direct and indirect methods are so different that it is impossible to compare them. Not only do they differ essentially in principle, but the type of results produced also varies. They should be regarded as complementary developments in radiological progress.

Future of Cineradiography

During the last few years great progress has been made in the quality of photographic materials, and in the speed of film emulsions, so that it is now possible to obtain first-class cinematographic films with the bone structure well defined. Exposures in the case of the thorax of normal individuals now occupy about one-fiftieth of a second. As to the length of exposure in any one case, a series of three 10-second exposures is often taken at one sitting, with perfect safety as regards any risk of over-exposure to the rays.

The advantages obtained from a permanent moving record of the organs of the body are obvious, not only for clinicians, but for workers in the allied medical sciences, particularly physiologists. Until recently radiology has been limited to the static rendering of shadows, with the exception of a screen examination, which is memorized and interpreted by the radiologist. Consequently diagnoses have had to be made on films taken at a particular instant. For example, the sign of persistent filling-defect in carcinoma of the stomach. Such diagnostic criteria will always be fundamental, but it is now possible to go a step further and make diagnoses on function also. The persistent deformity will remain, but the movements of the stomach and its response to standard technique will vary from the normal.

It will take time before additional methods of diagnosis are fully worked out, as the shapes and positions of any moving organ are almost innumerable, and we shall have to study the limits in the normal conditions in order to recognize the pathological. In other words, a moving radiographic physiology is now in process of evolution and a moving radiographic pathology may follow.

In the study of the normal and abnormal alike, cineradiography may in its turn be much enriched by the use of the sound track to combine with the photographic record a synchronized record of audible phenomena, such as the heart sounds, breath sounds, speech, and sounds produced by abnormal accumulations of fluid. In the study of the heart in particular the film may usefully incorporate a tracing of the electrocardiographic record, and possibly also of the record made by the 'densograph' or ionograph, an apparatus which gives a continuous measurement of the quantity of X-rays passing through any given part of the heart, and therefore of the thickness of the heart muscle at that point in any particular instant. The chief component of the ionograph is an ionization chamber filled with methyl bromide. The instrument gives valuable information when used in conjunction with the electrocardiograph. Unless there is a radical and far-reaching change in the method of production of X-rays, necessitating corresponding changes in the design of normal equipment, it is unlikely that the methods previously described for obtaining cineradiographic pictures will be altered except by improvement in details. The next few years will see great advances in cineradiography. It is not too much to say that, before long, physicians and surgeons may think as little of asking for a cineradiograph as they do now of asking for a normal photograph, and that, in suitable cases, cineradiography will take its place as a routine procedure. What has been stated above is little more than a brief summary of the more important applications of cineradiography. By means of a cineradiographic investigation it is possible to obtain a rapid, inexpensive and permanent record of the functioning of active organs and moving joints, and with continuous bands to study movements for an indefinite period, which has not been possible heretofore. The recording films may be used for (a) purely diagnostic purposes, (b) comparison with former records to study the effects of treatment, or the progress of the pathological condition; (c) teaching purposes; (d)

transmission from one place to another, for the purpose of obtaining specialists' opinions on the nature of the case; and (e) information as to the condition of the patient in the past, or for comparison with records taken at a future date.

Cineradiography opens an entirely new field for investigation, and provides valuable aid in medical diagnosis. Once the additional apparatus is installed, the method can be carried out without incurring any greater expense than would be necessary in an ordinary X-ray examination.

Kymography

Kymography is a technique which has been increasingly used during recent years for studying the X-ray appearances of the heart. Kymography, or the recording of movements by means of graphic curves, was first attempted by Sabat in Warsaw in 1911, and, about the same time, Goett and Rosenthal devised similar apparatus independently and obtained somewhat similar results. During the last ten years a great volume of literature on the subject has accumulated. The early workers were handicapped by the feebleness and uncertainty of the X-ray apparatus which was available to them, namely, the gas tube and induction coil. Coolidge's hot-cathode tube and an abundant supply of alternating current were not yet available. In 1925 Robert Knox, a great leader of radiology, read a paper on the subject at the first International Congress of Radiology. He was the first to suggest the extension of kymography from the investigation of the heart to that of the involuntary muscular movements of the gullet and stomach, oesophageal and gastric peristalsis. Perhaps one of the best known of modern workers in kymography is Stumpf of Munich, who has for the last ten years been perfecting a kymographic apparatus.

The latest form of the kymograph uses an ordinary large-size X-ray film—perhaps about 12 by 15 inches. The film is held in a vertical frame which occupies the position of the fluorescent screen, close to the patient's body. Between the film and the X-ray tube there is a thick lead plate pierced by a succession of thin horizontal slits, about 0.4 mm. wide and separated by regular intervals of about 12 mm. There is a mechanical device by means of which the film can be moved downwards for a distance corresponding to the distance between two slits, at a chosen rate of speed, while the tube remains switched on. Various workers give different exposures, but the most useful is about 3 seconds. The resulting picture is composed of a number of horizontal strips separated by black lines. Each of these strips corresponds to one of the thin slits, and it depicts the shadow of that part of the heart which was immediately opposite the slit. It shows the motion outwards and inwards of that part of the heart shadow during the period of exposure, beginning at the bottom, and ending at the top, in the form of a small wave. As Hirsch points out, the advantages of the translation of movement phenomena into wave-forms are obvious, it is the first step in the solution of the problem. The cardiologist then examines the picture minutely and infers, by accurate measurement and by comparison of the time and space characteristics of the various parts of the picture, the character of the movement at any point of the heart during the particular 3 seconds for which the film is exposed.

Kymography appears to be of definite use to cardiologists, but has by no means become a diagnostic method of choice, and is somewhat limited in its application.

Tomography

Tomography, planigraphy, and stratigraphy, are names given to those methods of radiography which aim at the delineation of a selected plane or

stratum of the patient's body. This is accomplished by moving the tube and the film during the exposure, in such a manner that the images of all objects in the selected plane occupy the same positions on the film, while images of objects in planes above and below that particular plane are blurred by the movements. After some experimental work by Bocage (1921-1935), and others, Grossman in 1935 devised an apparatus by which the technique was successfully developed. His apparatus and equipment are costly. In this machine the tube is carried by the upper end of a pendulum, the lower end of which, as it swings, moves a film-carrier attached to the lower end of the pendulum in the opposite direction. The axis on which the pendulum swings can be brought opposite to any desired plane of a patient's body, and objects in this plane are sharply defined on the film. About 1937, Twining designed a simplification of the apparatus, which was much less costly and gave a great impetus to this technique, and its use became much more general.

Tomography has been very useful in the X-ray examination of the thorax, especially for defining the presence of cavities or tumours, and giving an indication of their exact position. It has also been useful in the examination of special regions of the skull and of the spine. In special cases, this technique is invaluable for estimating the extent of lesions and their localization. Its one drawback is its expense, as in most cases a large number of films have to be used in ascertaining the exact plane in which the lesion is situated. Apart from this, it opens up a new and very valuable field in radiographical investigation.

Soft-tissue radiography

This is a valuable diagnostic technique, although there is no new principle involved in this form of radiographic investigation. Soft rays are employed, i.e. long wave-length radiation with comparatively little penetration of the tissues, so that the fleshy structures will cast relatively dense shadows. It is useful in the investigation of the structures of the nose, which is partly cartilaginous, or where certain tissues show partial calcification. It also helps in examination of the muscle planes in the limbs, and especially examination of the breast tissue in the female.

Radiography of joint spaces without introduction of opaque substances into joint cavities

Work has been done by Nordheim on the radiographic demonstrations of articular cartilages, especially the semilunar cartilages of the knee. The principle of the method is the creation of a vacuum in the joint space by an extreme passive movement. It is claimed that the internal semilunar cartilages of the knee can be demonstrated in 70 per cent of normal cases, and small intra-articular effusions can be visualized.

Ventriculography

This name is applied to the technique of introduction of air directly into the cerebral ventricles by means of a syringe and needle, after trephine openings have been made in the skull. A complete investigation of the ventricular system of the brain can usually be made in this way. It is of great value in the diagnosis of cerebral tumours and is now a standard technique.

Encephalography

This is the introduction of air into the sub-arachnoid space by lumbar puncture, or by the cisternal route. The air passes into the spaces in the sulci of the brain, and eventually finds its way into the ventricular system. In

Laruelle's Neurological Clinic in Brussels, encephalology has been practised as a routine method in the investigation of all cases of headache which do not arise from some simple cause. The patients are examined in the sitting position. A lumbar puncture is made, and 5 c.cm. of air are injected intrathecally. No cerebrospinal fluid is withdrawn. Films of the skull are taken almost immediately afterwards, and sufficient air is seen in the lateral and often in the third ventricle to detect any displacement of shadow or other gross abnormality.

The patient suffers no inconvenience, and is allowed to go home the same day. I have seen the examination made and have been much impressed by its simplicity and value.

Arteriography

Cerebral arteriography and cerebral angiography were first attempted by Egas Moniz of Lisbon (1927-1929) and has been practised in this country since 1931 at the National Hospital, Queen Square. When an opaque material, such as thorotrast (colloidal thorium dioxide) is introduced as a fluid into the internal carotid artery in the neck, and an X-ray film is taken immediately, while the fluid is passing through the carotid arteries, an opaque image is obtained of the intracranial vascular system. Usually 10 to 12 c.cm. of the suspension is used, but, if it is desired to obtain a view of the venous system as well, 15 to 17 c.cm. are necessary. The injection takes about 5 seconds, and the exposure must be rapid, about one-tenth of a second, made just as the injection is finishing for the arteries, and 2 to 3 seconds later for the venous system. Much valuable information is obtained by this method of investigation in the cases of suspected cerebral tumours or aneurysmal dilatation of the vessels. Arteries are sometimes seen to be displaced or obliterated by pressure. Although the thorium preparation is freed from radio-active mesothorium, yet the technique is not in favour now. It is only employed when the particular information desired cannot be obtained in any other way. The chief factors against its use are (1) A surgical operation is necessary to dissect out the carotid artery; this may be contra-indicated by the patient's condition. (2) The thorium dioxide may collect in the liver, spleen, and reticulo-endothelial system from which it is not eliminated. It may act as an irritant, and some workers have stated it may act as a carcinogenic substance.

The Lysholm grid

The modern Lysholm grid, designed by Lysholm of Stockholm, is a piece of apparatus which has proved of great use when fine detail is required, either in the screen image or on the film. The grid is an improvement on the Potter-Bucky diaphragm, being finer in structure; the metallic leaves are much closer together. It can be used as a stationary grid intercepted between the patient and the film, or the screen, when a screen examination is made; or it can be arranged so as to be movable and pass across the field at a uniform speed, as in the case of the standard Potter-Bucky grid. The important feature is the closeness of the grid lines which are often scarcely perceptible and do not interfere with the shadows. These grids cut out practically all scattered radiation and thus help in the production of a fine image.

Mass radiophotography (Photography of the fluorescent image)

This technique has made rapid progress during the last few years. Experiments were made during 1896 by Bleyer who constructed an apparatus,

which he called the photofluoscope, for photographing the screen image. This method was impracticable owing to the faintness of the screen image obtainable with the primitive X-ray apparatus, the comparatively narrow aperture of lenses, and the relatively insensitive plates then available, and so the method was abandoned. It was revived years later for the purpose of indirect cineradiography by Russell Reynolds in 1921 in this country. The development of both indirect radio-cinematography and radio-photography was made possible by improvements in X-ray generators and X-ray tubes, the highly luminous Levy-West fluorazure screens, and the manufacture of very wide aperture lenses and highly sensitive fine-grained films. Abreu (1938) developed a technique for obtaining miniature still films by photographing the fluorescent screen image. Potter suggested a film, 75 by 100 mm., for the purpose. A special fast lens was made, with an aperture of 1.5, such as is used for night photography from aeroplanes. Excellent reduced pictures of the chest were obtained in one-tenth of a second for adults, and one-twentieth of a second for children. The advantages are obvious, particularly in routine examinations of the chest. Large numbers of individuals can be examined in rapid succession, and the cost of the investigation is very considerably less than ordinary radiography. According to Potter, 1,000 chest films cost about £160 to produce, whereas 1,000 radio-photographs cost only £12. One of the chief advantages is in the economy of time. With well organized team work it is possible to examine with one apparatus 300 to 400 patients in an hour. The early recognition of pulmonary tuberculosis is very important and this technique admits of very large numbers of investigations being carried out with comparatively little cost. The Admiralty have already taken steps in this direction by instituting routine radio-photography for all the personnel in the Royal Navy.

Cooper gives an account of the mass survey of Army recruits during 1939. By March 1st, 1940, 22,000 men had been examined. A 35 mm. film was used. Every film was examined by at least one physician and one radiologist, usually more than two other medical men were present. Whenever anything abnormal was detected, a large radiograph (14 by 17 in.) was taken the next day and this was reported upon again by a physician and radiologist. When reading the small films they were projected up to a size of approximately 12 by 14 inches. The photographic unit in use consisted of a leica camera fitted with a F.1.5 lens focusing at 30 inches. It is obvious that this new technique is of sufficient importance to justify the hope that it will have a big future.

RADIOTHERAPY

Chronic interstitial mastitis

Superficial X-ray therapy, by which is meant the use of X-rays produced at a potential of 80-120 kv. such as is used for the treatment of skin lesions, has proved to be very successful in the treatment of chronic interstitial mastitis. Reynolds (1932), at the suggestion and with the active support of Sampson Handley, has treated many hundreds of such cases during the past few years, with success. The lesion rarely fails to yield to small doses. Individual cases naturally vary in their reaction to the particular dose given, but many will completely resolve after three doses of 250 r given at intervals of one week or ten days; in some cases six doses may be required.

Gilbert Scott's wide-field X-ray treatment

It has been observed for many years, long before the so-called deep X-ray therapy was practised, that in the treatment of superficial lesions, for example patches of psoriasis on the skin, individual patches which have not received

any direct radiation at all disappear. This may occur in the treatment of Hodgkin's disease; masses of granulomatous tissue or enlarged glands will resolve in a part at some distance from the actual area treated. This suggested that X-rays have a general effect on the body tissues quite apart from a purely local reaction.

Gilbert Scott advocates the use of X-rays as a therapeutic agent in small, widespread doses over the whole body, and designed a special X-ray tube for this express purpose. It enables a wide field to be irradiated at one time. In 1939 he mentioned an extensive range of diseases in which his method was applicable, for example inoperable masses of secondary growth in the abdomen, myelomatosis, asthma, and spondylitis *adolescens*, and reported marked success from this treatment, and especially insisted that only infrequent and moderately light doses are required, the patient's natural resistance to disease being thus unimpaired.

Regional X-ray baths

Walter Levitt, following the early work of Holzknecht (1905) and Dessauer (1907), and more recently of Chaoul and Lange (1923), obtained good results in the treatment of Hodgkin's disease and other radio-sensitive tumours, by giving what he terms regional X-ray baths (1929, 1939). High-voltage X-rays were used in the neighbourhood of 180-200 kv (180 kv with a filter of 0.5 mm. of copper or 200 kv with a Thoracur filter). Long-focus skin distances were necessarily used, 60-140 cm., according to the size of the field. The regional baths were either thoracic, abdominal, or trunk baths. In the thoracic and abdominal baths, treatment began with 35 and 25 r respectively, gradually increasing daily to 200 and 150 r respectively, until a total dosage of 1,000 r to each field was received. Good results were obtained in Hodgkin's disease, reticulosis, and metastases of testicular and other growths.

Super high-voltage therapy

This term describes the use of X-rays produced at a potential of 400-1,000 kv. The experience gained by this technique has been really very limited, chiefly because there are as yet only a few installations capable of such a high potential. Admittedly there are a number of 400 kv units in use, but very few of greater power even in America. The expense is very great and naturally limits production. The upkeep also is very costly, and it is almost universally admitted by physicists and radiologists alike that there is an economic limit as regards potential beyond which it is unwise to go. Generally speaking, 200 kv is considered as high a voltage as is necessary or even advisable. At this voltage X-rays of 0.62 Å wave-length can be produced. It is now generally admitted (Leucutia, Grove, and others) that if a lesion is unsuccessfully treated by irradiation with a 200 kv unit, radiation has failed in all cases in which a 500 kv unit has been used. At one time it was hoped that, by the use of very high potentials, it would be possible to produce gamma radiation of the same wave-length as that emitted by radium. So far this has not been practicable.

Chaoul's contact-therapy

Chaoul, in 1933, set up three conditions for treatment under the name of contact therapy, namely: soft radiation, short distance, and fractioning the dose. Chaoul used radiation of a half-value layer of 0.3 to 2.5 mm. of aluminium. For this penetration a tension of 45 kv peak to 65 kv peak was employed. Good results were obtained with a total dosage of 6,000-15,000 r, given in daily doses of 300 to 500 r.

A special X-ray tube is used so that the anode can be brought to within a few centimetres of the lesion. This short focal-skin-distance is the chief factor in confining the radiation effect in the tissues to a small volume. The tube is so constructed that it can be introduced into a cavity the base of which requires treatment, hence it must be shock-proof. The cathode is earthed and the anode is at a high potential. There is no inherent filter except the glass wall of the tube and its bakelite protective cap. At a tension of about 50 kv the total equivalent filter amounts to about 0.2 mm. of aluminium. Filtration is virtually the same in all directions, so that the isodose curves in free air are practically spheres around the focal spot. At the tension of 50 kv (contact), and a current of 2 ma, which current is allowable for continuous running, the intensity at 2 cm. from the focal spot is of the order of 8,000 r per minute. The apparatus is easily moved and can be used in the operating theatre. The diameter of the tube is about 1½ inches so that introduction into cavities is generally easily possible.

Special apparatus is not necessary when using it for superficial therapy so long as the therapist possesses a normal shock-proof X-ray tube which will allow the use of a small focal-skin-distance.

Short distance X-ray therapy has found a very definite place in therapeutic radiology. It is essentially a method of treating accessible lesions which can be brought into contact with the applicator of the tube, either by virtue of their situation or by previous surgical exposure, for example, epitheliomas, rodent ulcers, carcinomatous skin recurrences, carcinomas of the rectum, papillomas, keloids, naevi, pigmented moles, lupus, etc.

The advantages may be summed up as follows: (1) total energy absorption in small tissue volumes; (2) high dosage rate; (3) low cost. It has therefore to some extent replaced treatment with surface radium. The results were very striking and successful.

As to the future of diagnostic radiology, developments may be expected in certain directions. Particularly one may mention motion photography which would appear to be the only method available for ascertaining the functions of moving organs and the movements of joints.

The recent successful development of mass radiography—or the taking of miniature pictures—promises to have a big future in diagnostic radiography, especially when a very large number of systematic examinations have to be made from time to time, for example, examination of the lungs for evidence of tuberculous disease in the Services, and in large numbers of miners or others engaged in industrial work. It is also likely that further advances will be made in the use of opaque media for radiographic investigations in different parts of the body.

In therapeutic radiography, advances are being made in the use of X-rays as an agent for influencing biological processes of a beneficial nature in the human body, and in stimulating the tissues to resist disease rather than in the use of the rays as a destructive agent, as is at present the case.

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RECENT WORK IN ANAESTHETICS

By J. BLOMFIELD, OBE, M.D.

CONSULTING ANAESTHETIST, ST. GEORGE'S HOSPITAL, CHAIRMAN, ANAESTHETICS
COMMITTEE, MEDICAL RESEARCH COUNCIL, LONDON

POST-OPERATIVE PULMONARY COMPLICATIONS

Post-operative pulmonary complications are still a bugbear to both surgeons and anaesthetists, and it is doubtful if their incidence has been much lessened by the many modern improvements in anaesthetic practice. One of these, heavy premedication, is indeed by many authorities held to be responsible for numerous instances of pulmonary complications after anaesthesia. It is not, however, the method, but its application, which is at fault. It is well pointed out by Sircar and Boston that routine dosage must be avoided, that there must be a competent person to supervise the airway and general condition of the patient throughout the whole period of unconsciousness, and that post-operative sedation should be such that adequate relief from pain is secured with the minimum of respiratory depression. It is the general opinion that the type of operation has more influence than the anaesthetic agent on the tendency to post-operative pulmonary complications. Operations on the upper abdomen give rise to the condition in a much greater proportion than operations elsewhere in the body.

With regard to the influence of the anaesthetic itself it has often been held that ether is the agent most often to blame for pulmonary complications. This belief is not confirmed by analysis of very large numbers of operations. Sircar and Boston conclude that, given adequate premedication, the skilful administration of ether to patients without pre-existing pulmonary lesions does not lead to a higher proportion of post-operative pulmonary complications than does any other anaesthetic agent. In patients who already have lung trouble it is advisable to employ a non-irritating agent such as nitrous oxide or cyclopropane, but it is by no means certain that ether cannot be used with safety on these patients too, though active tuberculosis should certainly rule it out.

The deeper the plane of anaesthesia, the greater the liability to post-operative complications. This is due to depression of the respiratory centre which leads to shallow breathing, to intercostal paralysis, and to general loss of muscular tone. Even a short period of deep anaesthesia carries with it much greater risk of subsequent respiratory complications than does a much longer period of light anaesthesia.

Management of the patient after operation

This has much influence on the avoidance of pulmonary complications. If breathing is painful, as it commonly is after operations on the upper abdomen, sedatives must be used so as to give adequate relief with the minimum of respiratory depression. Until the reflexes have returned sufficiently to safeguard the patient against asphyxia or inhalation of foreign matter, either an airway must be used or safety assured by the patient's posture. A depressed patient must not be left long in any one position;

frequent change of posture is needed for adequate ventilation of all parts of the lungs. In an unconscious patient, in order to stimulate respiration, it may be advisable to add carbon dioxide to the inspired air; this is better than combining it with oxygen, for the nitrogen of air is not readily absorbed and so helps to prevent pulmonary collapse

THE RELATIVE SAFETY OF ANAESTHETICS

This is not easily determined, for the most reliable practical test in clinical results must be largely statistical, and is therefore to some extent both fallacious and slowly acquired. Laboratory determination of safety on the other hand, although it can estimate the effects of measured toxic doses of the anaesthetic, is valid only for the particular species of animal subjected to the experiment. It is pointed out that the conventional 'margin of safety' is unsatisfactory, because it is concerned only with the likelihood of overdosage, whereas it should also take into account the probability of resuscitation. The ease of resuscitation from overdosage depends on pharmacological considerations apart from those responsible for the 'margin of safety'. The term 'acute safety' is suggested for expressing both the 'margin of safety' and the probability of resuscitation. A given anaesthetic may be superior to another in the first, but inferior in the second. For example, divinyl ether is more rapidly eliminated than diethyl ether, and therefore more 'recoverable', but, as regards the circulatory condition of the patient at the time of respiratory arrest, diethyl ether is superior to divinyl, and has so far a better 'margin of safety'. All anaesthetic deaths result from overdosage and the failure to resuscitate. A formula for calculation of the 'safety index' gives mathematical value to the two properties which determine the immediate risk of anaesthesia, namely the probability of overdosage and the probability of failure to resuscitate. On this formula Draper and Whitehead find that diethyl ether is 96.0 safe, divinyl ether 100, and chloroform 9.5.

CYCLOPROPANE AS A ROUTINE ANAESTHETIC

The use of cyclopropane as a routine anaesthetic is sometimes deprecated on the ground that it is liable to cause ventricular fibrillation. There is no doubt that instances of this have occurred and been recorded, but experience so far suggests that the catastrophe is extremely unusual, and that it has not perhaps the inevitability of comparable accidents due to chloroform, and that in fact it may have been due to overdosage. Experimental cardiac irregularities during cyclopropane inhalation have been studied by Leech and Griffith who found that, though cyclopropane alone does not produce the phenomenon, when preceded by morphine it causes cardiac irregularities similar to those seen clinically. Arrhythmia is common under cyclopropane, but never dangerous if the gas is sufficiently diluted. It has recently been pointed out that the continuous inhalation of cyclopropane in dilution as weak as 2 to 5 per cent causes analgesia. The use of cyclopropane has become widely applicable, but only as the result of the introduction of the CO₂ absorption technique. This has proved of great service also in prolonged administrations of nitrous oxide and oxygen. Waters points out the importance of changing the soda-lime canister between cases, after exposure for some time the granules become coated superficially with carbonate which may surround the remaining alkali in their cores. If free from exposure for an interval the soda-lime again becomes active. The need for changing the soda-lime is generally shown by the patient's increased depth of breathing, and by rise of pressure within the closed system.

Draper and Longwell devised a CO_2 detector which is plugged into the inspiratory site of the closed circuit, and supplies a more accurate detection of the gas than if reliance is placed on symptoms alone.

HEADACHE FOLLOWING SPINAL INJECTION

The headache which sometimes follows spinal injection is an endless source of controversy among those who employ the method much. It is asserted by some to be a question of meningeal infection, and by others to depend on too great a withdrawal of cerebrospinal fluid or on too rapid an introduction of the anaesthetic solution; other explanations have also been offered. Treatment has been equally diverse. The latest recommendation is the application of X-rays (Schmerz-Narkos).

PRE-ANAESTHETIC DIETARY AND IMPORTANCE OF OXYGEN SUPPLY

The important part played by suitable diet before operation, as well as by adequate supply of oxygen both during and after anaesthesia, are explained in Reid's account of cellular respiration. Anaesthetic agents inhibit the efficiency of oxidation and of enzyme action. Pre-operative diet is therefore of great importance because, without an adequate supply of vitamin B_2 , there cannot be enough of respiratory carriers such as flavoprotein or the colozymes, since material necessary for their synthesis would not be available. Failures in oxidative processes which are in reality due to this deficiency have hitherto been explained in terms of circulatory disturbance, low haemoglobin, and allied changes. Most anaesthetics involve the enzyme, hydrogenase. The practical importance of utilizing the conception of cellular oxidation-reduction systems lies in its bearing on proper care of the pre-operative diet, particularly as regards its content of vitamin B_2 .

Equally logical from the point of view of cellular respiration comes the post-operative supply of oxygen which in some instances indeed is an imperative necessity. An adequate supply of oxygen during anaesthesia, as well as its supplementary use afterwards, is necessitated by the action which most anaesthetics exert on the hydrogenase.

ELECTRICAL ANAESTHESIA

Although electrical anaesthesia has now been of practical service in veterinary surgery for some years, it has not yet acquired more than theoretical interest so far as the human subject is concerned. Burge discusses the rationale of the method. An electric current of low amperage passes from positive scalp through galvanometer to negative forearm when a non-polarizable electrode is placed on the scalp as nearly over the motor area of the brain as possible. This current is decreased during rest and during sleep, but is increased by activity. Moderate exercise appears to charge the cerebral cortex preparatory to its emitting negative charges, or nerve impulses over the motor neurones. General anaesthesia blocks incoming sensory impulses, or negative charges, whereas outgoing negative charges are not blocked and can leave the brain; thus negative potential of the cerebral cortex is decreased. The synapse is the point at which the effect of the anaesthetic is manifested. It was hoped that, by decreasing the negative potential of the cerebral cortex by electrical means, general anaesthesia could be brought about. So far, however, no such attempt has been successful.

ETHER CONVULSIONS

Instances of that still unexplained phenomenon, ether convulsions, continue to crop up with some frequency, but do not shed any further light on its causation, although they often serve to destroy hypotheses already formulated. For example, the most recent subject of convulsions, well observed under favourable conditions, gave positive evidence against the suggestion that convulsions are due to low calcium-content and should be treated by calcium injections. This girl was not apparently benefited at all by intravenous administration of calcium gluconate during the seizures, and on a second occasion when ether was given without any adverse symptom the serum calcium was lower than on the occasion when convulsions occurred. Experimentally calcium chloride allays convulsions caused by procaine; it acts by rendering tissue membranes more impermeable, thus preventing the rapid diffusion of the poison and protecting the cerebral centres. Local anaesthetics are rapidly-striking drugs which must be kept away from the brain centres. The new method of achieving this depends on increasing impermeability by the use of calcium salts.

ANAESTHESIA IN YOUNG CHILDREN

The best method to adopt for getting and maintaining anaesthesia in young children (Sington) is a matter on which there is difference of opinion even between those who are equally expert in their practices. Thus some authorities regard it as almost criminal not to precede the actual administration by a sedative or hypnotic, whereas other equally proficient anaesthetists believe that this is an unnecessary and often a harmful procedure. Sington lays down two axioms for induction in a child, namely that he should always be sitting up, and that restraint of any kind should not be used. Obviously this does not apply to the very young, for with an infant it is almost always necessary to let him have someone with whom he can busy his hands, and he is generally more ably managed lying down than sitting up when he tends to flop. For all more stable children Sington's advice is admirable, and it presupposes the essential element for success in that the child is treated like a rational being, and with perfect openness and confidence. Generally speaking, simple methods are most suitable for children, but for special operations, such as cleft palate, there is no shadow of doubt about the advantages of the endotracheal method and appropriate apparatus.

NITROUS OXIDE ANAESTHESIA

A new light is shed on the effects of nitrous oxide anaesthesia by the work of Courville, and anaesthetists will be brought to realize that there are dangers which have long been unsuspected in the use of this gas which has hitherto been thought to be the very type of a 'safe' anaesthetic. It is the employment of nitrous oxide for prolonged operations which has brought the truth to light, for during short operations nitrous oxide is, as has always been supposed, really safe unless gross restriction of air or oxygen is involved. The danger in prolonged operations is that an amount of anoxaemia may be allowed to persist which, scarcely obvious at the time, is yet enough to produce serious damage. When nitrous oxide, through asphyxia, is fatal at a short operation, the effect is immediate. Such instances are rare, and should be entirely avoidable. Generally speaking it may be said that they occur only when the patient is the subject of some intercurrent lesion rendering him unusually vulnerable. Long operations provide a different

problem. The sequelae to these, due to prolonged inhalation of nitrous oxide with insufficient oxygen supply, may, according to Courville, be: (1) Death after a short period which does not allow of the appearance of the characteristic necrosis of cerebral grey matter, pulmonary oedema is the rule in these patients. (2) Death after a prolonged survival period. (3) Recovery with residual symptoms indicating cortical or lenticular damage. (4) Transitory mental and emotional manifestations.

The troubles are not due to the toxic quality, which is slight, of nitrous oxide, but solely to the anoxaemia incident to its provision as an anaesthetic with limited air or oxygen accompaniment. That this is true Courville demonstrates by the histological evidence from fatalities. The findings characteristic of excessive narcosis—destructive action limited to the nerve cells and multiple petechial haemorrhages of the centrum due to damage to the capillary endothelium—are absent in the brains of those who die from nitrous oxide inhalation. In them the appearances are those which are seen in the brains of experimental animals after temporary ligation of arteries supplying the brain, and are assumed to be due to oxygen want. There are areas of devastation in the brain where interstitial elements as well as the nerve cells and fibres are damaged. Moreover, the lenticular nucleus is particularly affected, a characteristic feature of asphyxia. In short, the contention is that 'anoxaemia of a variable degree accompanies nitrous oxide-oxygen anaesthesia, and that various complications, often serious and too frequently fatal, are due to the effects of oxygen want on the brain. The author gives full records of the patients on whose symptoms and lesions he bases his argument. It seems to be proved that in the past there have been both fatalities and mental injuries which, really due to nitrous oxide inhalation, have never been truly ascribed

CHEMICAL PATHOLOGY

By JOHN MARRACK, D.S.O., M.C., M.D.

PROFESSOR OF CHEMICAL PATHOLOGY, UNIVERSITY OF LONDON, CHEMICAL
PATHOLOGIST, LONDON HOSPITAL

INORGANIC CONSTITUENTS OF BLOOD

The importance of the maintenance of a normal total base concentration in the extracellular fluids of the body has been fully appreciated only since the discovery that reduction of the total base in plasma is a constant feature of Addison's disease (Allott). The total base concentration in plasma normally lies between 150 and 164 mille-equivalents per litre, average 155. It is made up as follows:

Sodium	143	mille-equivalents	per	litre
Potassium	5	"	"	"
Calcium	5	"	"	"
Magnesium	2	"	"	"

Sodium

Since sodium forms the greater part of the total base, variations of the total base concentration outside of normal limits occur only as a result of variations of sodium. In the Goulstonian lectures (1936) McCance gives an entertaining review of mineral metabolism in relation to medicine and describes experiments on normal persons which show the results of a simple sodium deficiency, without the confusing effects of other abnormalities. The symptoms—weakness, languor, nausea, and loss of appetite—resembled those of Addison's disease. The loss of sodium in Addison's disease is due to increased permeability of the kidneys (Cutler *et al.*).

The plasma sodium may be reduced in any condition in which there is an excessive excretion in the urine or loss of body fluids (McCance). An interesting example is that produced by excessive sweating. In the ketosis of diabetes mellitus there may be a serious depletion of base as well as anhydraemia; when the volume of blood is restored, on treatment, the base concentration of the plasma may further be reduced unless salt is supplied freely. The plasma base may be low in various febrile conditions also, such as pneumonia and tuberculosis. These observations indicate the importance of giving patients sufficient salt; a pint of milk supplies only about 0.3 g. of sodium; more than this may be lost in the sweat in an hour.

Potassium

An increase in the concentration of the potassium in plasma, not, however, comparable to that seen in Addison's disease, has been found in allergic conditions (Hoffman and Jacobs; Rusk *et al.*). Scudder attaches importance to variations of plasma potassium in conditions of shock; but severe shock may occur when the plasma potassium is normal.

Plasma potassium normally falls after ingestion of large amounts of glucose and may be much reduced when diabetic patients are treated with

insulin (Harrop and Benedict). Abnormal reduction after ingestion of glucose has been observed (Aitken *et al.*, 1937) in a patient with familial periodic paralysis; an attack of paralysis occurred when the plasma potassium fell to 10 mg. per 100 c.cm. The drop in the plasma potassium is not the sole cause of the paralysis, and reduction to this level may occur in other cases without paralysis.

Calcium

There has been a prolonged controversy about the state of calcium in plasma. The results obtained by the frog heart method of McLean and Hastings throw the weight of evidence in favour of the view that the greater part of the diffusible calcium is in the form of calcium ions. When either calcium or phosphate concentration is raised above normal levels in vitro or in vivo non-diffusible aggregates of calcium phosphate are formed (McLean and Hinrichs). These aggregates are removed from the plasma and can be detected in the phagocytic cells of the liver and spleen (Gersh). Boynton and Greisheimer give valuable data on the variations of calcium in the plasma of normal persons.

Magnesium

The occurrence of a form of tetany in cattle (e.g., milk tetany in calves, Duncan *et al.*), due to low concentration of magnesium in the plasma, suggests the possibility that some forms of neuromuscular hyper-irritability in man may be due to the same cause. Hirschfelder observed that twitching in patients with renal failure might be associated with concentrations of plasma magnesium below 1.4 mg. per 100 c.cm.

Hirschfelder also found that patients with nephritis excrete magnesium slowly, and the magnesium in the plasma may rise to 10 mg. per 100 c.cm. after a dose of magnesium sulphate. Coma occurs in animals when the plasma magnesium is raised above 17 mg. per 100 c.cm. It may be that some of the symptoms of renal failure may be produced by treatment with magnesium sulphate.

VITAMINS

The Vitamin-B complex

The part played by vitamin B₁ in the metabolism of glucose is mentioned by Harris in his review (1939). It is now established that one of the functions of two other vitamins of the B complex, riboflavin and nicotinic acid, is to act as 'middlemen' in the transfer of hydrogen from glucose (or intermediate products of the break-down of glucose) to atmospheric oxygen. In the old terminology they act as carriers of oxygen for the oxidation of glucose. For this purpose they are combined in compounds resembling nucleoproteins.

Vitamin B₁ (Aneurine)

When vitamin B₁ is deficient, the further break-down of pyruvic acid, an intermediate product of the break-down of glucose, fails. Platt and Lu showed that ketonic substances, which combine with sodium bisulphite (bisulphite binding substances, B.B.S.), are increased in the blood of patients with acute beri-beri and fall to normal levels on treatment with vitamin B₁. The B.B.S., however, are not constantly raised in the blood of subacute cases. They do not rise in the blood of normal persons who have taken a diet deficient in vitamin B₁ for three weeks, although symptoms of deficiency develop, nor in the blood of patients whose diet is deficient in B₁ (Robinson *et al.*, 1940, b).

Pyruvic acid forms a fraction only of the B.B.S. in blood. Pyruvic acid itself

can be estimated by a fairly simple method (Lu); the amounts found in the blood by this method were:

	<i>mg. pyruvic acid per 100 c.cm.</i>		
Cured and resting cases	Range 0.4 to 0.75	Mean	0.55
Subacute beri-beri	„ 0.77 to 1.93	„	0.93
Fulminating beri-beri	„ 1.00 to 5.77	„	2.72

Vitamin B₁ can be estimated in the urine by various methods (Wang and Harris; Melnick, 1939). Interfering substances cause difficulties in methods based on fluorescence of thiochrome. The method of Wang and Harris appears to avoid most of these difficulties and to be suitable for clinical use. Several authors since Harris and Leong have found that the level of excretion in the urine might be used as a test for vitamin deficiency. Melnick, Field, and Robinson, and Robinson *et al.* (1940, a) consider a daily excretion of not more than 90 μg by males and 53 μg of aneurine* by females as evidence of deficiency. However, Wang and Harris, Melnick and his colleagues, and Hills consider that it is more satisfactory to measure the amount excreted after a test dose. When 5 mg. of crystalline aneurine hydrochloride is given by the mouth after a meal, the amount excreted in the urine during the next 24 hours should rise by at least 0.35 mg. above that excreted in the 24 hours before the dose (Melnick, Field, and Robinson, Robinson *et al.*, 1940, a and b). The response to the test, however, is sometimes high when the amount of B₁ in the diet has been less than optimal.

The estimation of vitamin B₁ in blood by Meiklejohn's method, depending on the promotion of growth of the fungus *Phycomyces blakesleeana*, and by other methods is discussed by Sinclair. He concludes, from the analysis of the blood of 74 normal adults, that the apparent normal range of B₁ is from 8 to 15 μg per 100 c.cm., with a mean of 10.6 μg ; values below 7 μg can be considered abnormally low. He gives a method of correction for the adjuvant action of blood on the growth of the fungus and of calculating the true B₁ values.

Riboflavin, vitamin B₂ (G)

Normally about 1 mg. of riboflavin is excreted per day. Emmerie (1936, 1937) found that the amount excreted is reduced when the riboflavin in the diet is diminished and increased after eating liver or taking pure riboflavin. Methods based on the fluorescence of riboflavin can be used for its estimation in urine (Ferrebee). It is possible that riboflavin deficiency may be detected by measuring the response to a test dose.

Nicotinic Acid

Over 3 mg. of nicotinic acid are normally excreted in the urine daily. Nicotinic acid in urine can be estimated by the method of Harris and Raymond, preferably with modifications according to Kodicek. Harris and Raymond showed that after a test dose of nicotinic acid the excretion is increased; also that, in a few cases in which the intake was low, the excretion was less than normal. The value of the method as a test of nicotinic acid deficiency has not been tried. The concentration of nicotinic acid in the blood is not reduced when the amount in the food is low.

Vitamin C (Ascorbic Acid)

Tests for vitamin-C deficiency were described by Harris in Vol. XII, p. 584. Harrison, Mourant, and Wormal, using the rapid method of Harris and

* The international unit of vitamin B₁ is now 3 μg . of crystalline aneurine hydrochloride.

Abbasy, found evidence of serious deficiency in a small proportion only of normal medical students.

The methods of estimating ascorbic acid in plasma appear to be trustworthy. Amounts exceeding 0.8 mg. per 100 c.cm. are not found unless the amount of vitamin C in the preceding diet has been satisfactory; but lower values may occur when small amounts have been taken in the period immediately preceding the examination. The amount of ascorbic acid in the red blood corpuscles is a better index of the state of nutrition of the subject. However, different methods of estimating ascorbic acid in blood and red blood corpuscles give discrepant results. Butler and Cushman discuss these methods and describe a technique which appears to be satisfactory.

Vitamin D

The phosphatase is constantly raised in the plasma of patients with active rickets, but it appears that elevation of plasma phosphatase is not proportional to the severity of the disease and cannot be used as evidence of vitamin-D deficiency (Morris *et al*)

Vitamin A

Estimation of carotenoids and of vitamin A in blood has been used as a chemical method of demonstrating vitamin-A deficiency. Thus de Haas and Meulemans found very small amounts in the plasma of children in Batavia with xerophthalmia. Steininger and others review the subject, from the results of their investigations they conclude that the level of vitamin A and carotenoids in the blood, at any time, does not necessarily reflect the level of the stores of vitamin A but should do so unless there has been an abrupt change in the diet.

LIVER FUNCTION

Tests

Since tests of liver functions were discussed by Aitken in Vol. VIII, Quick's (1936) hippuric acid method has come into general use. This test depends on the fact that glycine, required for conjugation with benzoic acid to form hippuric acid, is produced by the liver. After a dose of 6 g. of sodium benzoate, 3 g. of benzoic acid combined as hippuric acid (benzoyl-glycine) are normally excreted in the urine in 4 hours. The estimation of hippuric acid is easy, and the test more convenient than other functional tests, except the estimation of bilirubin in plasma and the rough measurement of excess of urobilinogen-urobilin in urine. Its application is discussed by Snell and Plunkett, and by Kohlstaedt and Helmer. Using this test Bartels found evidence of impaired liver function in conditions of hyperthyroidism, the degree of impairment shown by the test bore little relation to the degree of elevation of the basal metabolic rate.

It is claimed that the degree of retention of bilirubin in the plasma after intravenous injection (see Vol. VIII, p. 84) is the most sensitive of liver function tests, but, as it may give evidence of severe impairment of function in the later stages of normal pregnancy (Soffer, 1938), its value is questionable.

The fructose (laevulose) tolerance test (see Vol. VIII, p. 84) is improved if the concentration of fructose is estimated, rather than the total blood sugar (Herbert and Davison, Herbert). The advantages are that the blood fructose does not rise abnormally in diabetic patients after a dose of fructose and that conclusions are drawn from an absolute measurement of blood fructose and not from a difference, possibly small, between two measurements of blood sugar. In about 80 per cent of normal and non-hepatic cases the blood

fructose per 100 c.cm. does not rise by more than 10 mg. and in none by more than 15 mg. When the liver is severely damaged the increase may be over 20 mg.

Salt has proposed that the excretion of glucuronic acid after a dose of aspirin might be used as a test of liver function. He gives an improved method of detecting glucuronic acid in the urine. As a small fraction only of salicylic acid derived from aspirin is conjugated with glucuronic acid, it is doubtful if this test will do more than detect normal variations of this fraction.

Prothrombin and Vitamin K

This subject has been reviewed by Quick (1940). For the formation of prothrombin by the liver it is necessary that (i) the supply of vitamin K should be adequate; (ii) the vitamin K should be absorbed from the intestine—this requires the presence of normal bile and a normal intestinal wall, (iii) the liver should not be too severely damaged.

According to Mellanby's simple theory of blood clotting, the enzyme thrombin is formed by the action of thrombokinas (or thromboplastin) on prothrombin in the presence of calcium ions, thrombin converts fibrinogen into fibrin, which forms a clot. In order to demonstrate a deficiency of prothrombin by the delay in the clotting of plasma, the concentration of calcium ions must be optimal and thrombokinas in excess, so that the concentration of prothrombin is the limiting factor. When blood clots in the ordinary way, the thrombokinas concentration is low and is therefore the limiting factor. Various methods are used, for example those of Quick (1936, 1938) and Smith *et al.* That described by Illingworth is simple.

The thrombokinas is conveniently prepared from dried brain. The clotting time of normal plasma with different preparations of thrombokinas varies. The clotting time is not inversely proportional to the concentration of prothrombin in the plasma, it is slightly prolonged when the concentration is halved, and is about five times as long as normal when the concentration is reduced to one-sixteenth. The prothrombin concentration can be derived from the clotting time by a table, obtained empirically. It is more convenient to use the prothrombin index:

$$\frac{\text{Clotting time of normal plasma}}{\text{Clotting time of patient's plasma}} = 100$$

Severe haemorrhage is likely to occur when the index is below about 50 or the prothrombin below about 20 per cent of normal.

The prothrombin concentration is remarkably constant in the plasma of normal persons. Kark and Lozner have described cases in which deficiency of vitamin K in the diet caused reduction of plasma prothrombin.

The plasma prothrombin is reduced in various forms of liver disease (Butt *et al.*). The prothrombin index can usually be raised by the administration of vitamin K by the mouth. In order to ensure absorption bile salts are given at the same time. In primary liver disease there may be no response to this treatment as the liver is not able to make prothrombin (Snell and Butt).

Vitamin K has been shown to be a naphthoquinone derivate; one form is 2-methyl-3-phytyl-1:4-naphthoquinone. The long phytol tail is not essential and the synthetic compound 2-methyl-1:4-naphthoquinone can be used instead. MacFie *et al.*, and Andrus and Lord injected this compound intramuscularly and obtained excellent results although Butt *et al.* found that the effect of natural vitamin K, injected intramuscularly, was not striking.

The prothrombin in the plasma of new-born infants falls after the first day and usually rises again in one or two days (Waddell *et al.*; Quick and Grossman; Dam *et al.*). If the recovery is delayed haemorrhages may occur. The condition can be cured with vitamin K; it has also been treated successfully with 2-methyl-1:4-naphthoquinone (Nygaard).

KIDNEY-FUNCTION TESTS

The urea clearance test (Peters and van Slyke) is now recognized as the most satisfactory of kidney function tests in general use. Objections to the test do not lie so much in the theory of the test as in the practical application. All tests that depend on the accurate collection of the urine secreted in a given time demand either catheterization of the patient or co-operation by patient and nursing staff that cannot always be attained. Giving a dose of urea before the test (Fowweather) is less unsound theoretically than might appear at first sight, it makes a free diuresis more likely and therefore reduces the percentage error in the volume collection per hour. When doubt is felt whether it is possible to collect the urine passed per hour accurately, Harrison's test (1922), which makes no allowance for volume of urine, may be more satisfactory. As the volume of urine passed per hour falls, it makes progressively less difference to the ratio of urea concentration in blood to urea concentration in urine.

The theories of the excretion of urine, on which such tests are based, are discussed by Smith (1937). Urea is excreted in the filtrate from the glomeruli but it is reabsorbed in the tubules. The urea clearance therefore measures the result of two opposing processes. In order to be able to measure the one process, filtration through the glomeruli, a search has been made for other substances which are neither excreted nor reabsorbed by the tubules. According to Shannon and Smith the polysaccharide inulin is excreted only by the glomeruli and is not reabsorbed. The inulin clearance after intravenous injection of a solution of inulin is therefore regarded as a true measure of the rate of filtration through the glomeruli. Severe reactions have occurred after intravenous injection of inulin (McCance). Smith (1938) describes a method of purification by precipitation with alcohol and filtration through a Seitz filter. Using inulin purified in this way only 5 reactions which could be ascribed to the inulin occurred after 168 injections; of these 5 only 2 were severe.

The controversy about the nature of the substance in human plasma that reacts like creatinine with alkaline picrate appears to be settled by the work of Miller and Dubos. The greater part of the chromogenic material in normal plasma is actually creatinine. When the creatinine concentration in plasma is raised considerably, after a dose of creatinine taken by the mouth, it may be assumed, with very little error, that all the apparent creatinine is actual creatinine. The creatinine clearance can be calculated on this assumption. This creatinine clearance (exogenous clearance) is higher than the inulin clearance; Shannon considers that creatinine is not only filtered off in the glomeruli, but also excreted by the tubules. Miller and Winkler estimated the creatinine clearance when no dose of creatinine had been given; they found that the clearance under these conditions (endogenous creatinine clearance) is less than the exogenous clearance and equal to the inulin clearance. The more obvious explanation is that the apparent creatinine is not all true creatinine and that part is not excreted.

The sugars sucrose and xylose are not metabolized when injected intravenously and can therefore be used for clearance tests. They appear to be reabsorbed to some extent in the tubules.

Cope, and Winkler and Parra, compare the clearance of various substances by normal and diseased kidneys. It is possible that the use of one of these substances will prove more satisfactory than urea, both theoretically and practically, for kidney function tests. For the present the urea clearance seems to be the most convenient test and has the advantage that very extensive studies of its variations in health and disease have been made.

Phenolsulphonephthalein (P.S.P.) is excreted by the tubules (Marshall; Shannon). The P.S.P. test of kidney function, as usually made, is not as delicate a test as the urea clearance and liable to error owing to inaccurate timing of specimens. Chapman and Halsted consider that it can be made more satisfactory by collecting the urine passed at 15, 30, 60, and 120 minutes after injection.

BRAIN METABOLISM

The respiration of the central nervous system is the subject of two reviews by Quastel. The brain burns little besides glucose, the respiratory quotient is nearly 1. The rate of oxidation falls when the oxygen content of the blood supplying the brain is reduced, unconsciousness results when the oxygen saturation of the blood falls to 24 per cent. Oxidation in the brain is inhibited by narcotics. But the degree of inhibition brought about by a narcotic dose varies with the type of narcotic; inhibition of oxidation is, therefore, probably not the primary cause of narcosis.

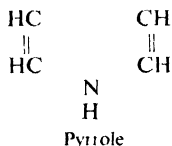
Reduction of the blood sugar by insulin also reduces the rate of oxidation in the brain, owing to lack of the only fuel that the brain can burn. Hypoglycaemia therefore has the same effect as anoxaemia, and prolonged hypoglycaemia, like prolonged anoxaemia, causes permanent damage. Maddock *et al.* and Hinrich *et al.* have studied the relation between the fall of blood sugar and the cortical potentials.

The concentration of glucose in the cerebrospinal fluid falls more slowly, after insulin, than that in the blood, before the injection, the concentration in the blood is usually higher than in the cerebrospinal fluid; but in an hour after the injection of insulin the concentration is higher in the cerebrospinal fluid, and remains higher during the period of hypoglycaemia (Day *et al.*).

Kerr and his colleagues have shown that the nervous symptoms of insulin hypoglycaemia are not related to the level of glucose in the blood or cerebrospinal fluid, but to the glycogen concentration in the brain. Thus cats are prostrated and are liable to coma when the glycogen in the brain falls from the normal level of about 100 mg. per 100 g. to about 58 mg.

HAEMOGLOBIN METABOLISM

A short and useful review of porphyrin metabolism is presented by Rimington (1939). A porphyrin molecule is built of four pyrrole rings, formed into a



large ring by bonds joining the C atoms adjacent to the N atom; this ring is very stable. The hydrogen atoms of the remaining two C atoms of each pyrrole ring are substituted by other groups. The porphyrins are classed

into 4 series, I, II, III, and IV according to the order of arrangement of these substituents. These can be represented diagrammatically as follows, A and B representing substituent groups

A	B	A	B	A	B	A	B
B		A	A	B	A	A	B
A		B	B	A	B	B	A
B	A	B	A	B	A	A	B
I		II		III		IV	

Porphyrins of series I and III only have been found in nature. A porphyrin of one series cannot be converted, *in vivo*, into one of another series. Proto-, copro-, and uro-porphyrins differ in the nature of the substituents. There can be a proto-, copro-, or uro-porphyrin of each series.

The porphyrin of haemoglobin, myoglobin, catalase, and cytochrome is protoporphyrin of series III. The iron atom is attached to the N atoms of the pyrrole rings. Normally small amounts of porphyrins of series I and III are excreted. The porphyrin of series I cannot be formed from protoporphyrin III and it is suggested that it is a by-product in the synthesis of protoporphyrin III. When the rate of formation of haemoglobin is increased, as, for example, to make up for an increased rate of breakdown of red blood corpuscles, the amount of this by-product rises: e.g., from the normal daily excretion of 0.03 mg. in the urine and 0.2 mg. in the faeces, to 0.15 mg. in the urine and 0.7 mg. in the faeces.

There has been some question about the cause of the cyanosis in patients treated with drugs of the sulphanilamide series. The chief cause of the dark colour of the blood appears to be methaemoglobin. The removal of cyanosis by treatment with methylene blue (Hartmann *et al.*; Wendal) was in agreement with this supposition. However, Marshall and Walzl, and Ottenberg and Fox suggested that the darkness of the blood was due to the presence of coloured products of the drug itself. Since that time various investigators (Wendal *et al.*; Vigness *et al.*; Fox and Cline) have found no evidence of such products of these drugs in the blood of human subjects. The colour of the blood is due mainly to the presence of methaemoglobin, which may form as much as 24 per cent of the total haemoglobin. In some cases smaller amounts of another pigment, which is usually supposed to be sulphaemoglobin, are also found. Drugs of the sulphanilamide series, including sulphapyridine, cause an increased excretion of porphyrin (Rimington, 1938, 1940). This porphyrin belongs to the III series and appears therefore to be not a by-product in the synthesis of haemoglobin but an abnormal product of the breakdown of haemoglobin. The main product of the normal breakdown of haemoglobin is bilirubin, in the molecule of which 4 pyrrole rings are joined in an open chain. The ring of pyrrole is opened before the protein and iron of the haemoglobin are removed: no iron- and protein-free porphyrin is formed in the process. It is possible, however, that methaemoglobin is broken down, in a different way, with the formation of porphyrin.

Treatment with sulphapyridine may give rise to a haemolytic anaemia. In this event the excretion of urobilinogen and urobilin in urine and faeces is increased, for example to 0.9 g. instead of normal amounts of about 0.1 g. (Erf and MacLeod).

PROTEINS OF PLASMA AND URINE

It has long been known that the globulin in the plasma is increased in infections and in malignant disease. More recently it has been realized that the rate of sedimentation of the red blood-corpuscles depends on the nature of the plasma proteins, which must therefore be altered in some way in most diseases. Evidence has accumulated to show that antibodies are proteins. The possible chemical and physical changes that may be associated with these changes of amounts and properties of plasma proteins call for consideration.

Until recent years the methods by which proteins of body fluids could be studied were extremely crude, but newer and more delicate techniques are now beginning to bear valuable fruit.

It has been felt for some years that the method of separation of serum protein into fractions by precipitation with salts in high concentrations was unsatisfactory. Hewitt (1938) found that a protein fraction, with the characters of a globulin containing a large amount of carbohydrate, is present in the fraction of serum protein not precipitated by half saturation with ammonium sulphate. This protein differs from albumin, which contains very little carbohydrate, and resembles serum globulin.

The Svedberg ultra-centrifuge introduced a method of separating proteins according to their molecular weight. The most probable explanation of the observations of McFarlane is that globulin molecules split up to some extent in the presence of protein of smaller molecular weight, and that molecular weight is no criterion of chemical differences. His investigations, however, suggest the presence of abnormal proteins in pathological sera and urines.

On the other hand, the separation effected by cataphoresis depends on a definite chemical difference between proteins. With improved technique Tiselius showed that horse and rabbit sera contain three globulin fractions, α , β , and λ . The rates of movement in the cataphoresis apparatus at pH 8 are in the order $\alpha > \beta > \lambda$. The iso-electric point of the λ fraction is at pH 6.0, those of the α and β fractions at pH 5.1. Using this method it was shown that a quarter of the fraction which was not precipitated by 55 per cent saturation with ammonium sulphate, the so-called albumin fraction, was globulin; the fractions precipitated by the lowest concentration of salts contained both β and λ fractions.

Tiselius (1937) and Tiselius and Kabat (1939) found that antibodies to egg albumin and pneumococci in the sera of rabbits and monkeys moved largely with the β fraction; but diphtheritic-antitoxin and other antibodies in horse serum form a fraction, hitherto unknown, with a mobility between those of the β and λ fractions (Pappenheimer *et al.*).

Several investigators, Stenhagen, Blix, Kekwick, found that human plasma contains the three globulin fractions α , β , and λ . The most significant change found in pathological sera is that the reduction of albumin in nephrotic serum is much greater than salt precipitation methods indicate (Longsworth, Shedlovsky, and MacInnes; Longsworth and MacInnes; Luetscher, 1940). Although these methods of estimating albumin in serum do not give grossly inaccurate results when the albumin concentration is not much reduced, they give results that are far too high when the albumin concentration is very low and globulin little affected. Ninety per cent of the protein in the urine of nephrotic patients may be albumin, and the concentration of albumin in the urine may be 80 per cent of that in the plasma. As the total plasma of an adult may contain as little as 12 g. of albumin, a large proportion of the total plasma albumin may be lost in the urine each day.

According to Newell and his colleagues the antibody to staphylococcus haemolysin and to ragweed are carried in the β globulin fraction of human serum.

Luetscher (1939) found that the albumin of human serum could be separated into two fractions α and β ; at pH 4 the α fraction moves faster than the β fraction. Normally the ratio of α to β fraction is about 2 to 1; but in nephrosis and cirrhosis of the liver α is reduced more than β . Apparently, when much albumin is lost in the urine or the liver is damaged, the β fraction is regenerated more quickly than the α fraction.

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PART II
DRUGS

RECENT DEVELOPMENTS IN DRUG THERAPY

By W. J. DILLING, M.B., CH.B.
PROFESSOR OF PHARMACOLOGY AND GENERAL THERAPEUTICS,
UNIVERSITY OF LIVERPOOL

THE WAR AND SUPPLIES OF DRUGS

The majority of raw materials from which medicines are prepared have to be brought to this country by sea and in consequence since war began imports have been greatly reduced and prices have advanced. With nearly all crude drugs the rise in price has been substantial and does not appear to have reached its highest level. Medicinal fine chemicals are also dearer but as they are manufactured in Great Britain adequate supplies of most of them are available, and the prices of these products, as a group, although higher than pre-war, have not advanced to anything like the same extent as have the prices of vegetable drugs.

In order to maintain supplies of essential synthetic drugs which were protected by patents held by German firms, licences have been granted for their manufacture by British firms: these drugs have previously been known by registered trade or proprietary names and, in the hope of securing uniformity in their new nomenclature, the British Pharmacopoeia Commission announced the official pharmacopoeial titles for these drugs. Unfortunately, in some instances fresh proprietary names have been evolved by the new manufacturers, such additional synonyms create confusion and it is therefore incumbent upon the medical profession to prefer the official pharmacopoeial title when ordering these drugs.

In the following list the official pharmacopoeial titles precede the proprietary or 'brand' names which are within brackets: bromethol (avertin), a basal hypnotic; carbachol (doryl, choryl), a parasympathetic stimulant; hexobarbitone soluble (evipan sodium, cyclonal sodium, hexanastab), an intravenous anaesthetic; iodoxyl (uroselectan B, pyelectan, uropac), for radiological examination of the kidney; leptazol (cardiazol, metrazol, phrenazol), a stimulant of the respiratory and vasomotor centres; mepacrine hydrochloride (atebrin, quinacrine) and mepacrine methanesulphonate (atebrin musonate), for the treatment of malaria; nikethamide (coramine, anacardone, nicamide), a stimulant of the respiratory and vasomotor centres; pamaquin (plasmoquine, praequine), for the prophylaxis and treatment of malaria (sexual parasites); phemitone (prominal), for the treatment of epilepsy; stibophen (fouadin), for the treatment of schistosomiasis, and suramin (germanin, Bayer 205), for the prophylaxis and treatment of trypanosomiasis. These preparations, with the exception of pamaquin and suramin, received official status through the Third Addendum (January 1, 1941) to the British Pharmacopoeia, 1932.

The Second Addendum (June 14, 1940) to the British Pharmacopoeia, 1932, contains preparations which will become increasingly important as sources of vitamins A and D, and official recognition is given to tetanus toxoid as an immunizing antigen: these additions will be discussed in more detail later. The Addendum also authorizes the substitution of arachis, cotton-seed, or sesame oil for olive oil in making linimentum camphorae, unguentum aquosum, and unguentum hydrargyri compositum; unguentum simplex, prepared with yellow soft paraffin, may be used in place of the yellow beeswax and benzoinated lard in making unguentum acidi tannici; and also in place

of the lard, hard and yellow soft paraffin in making unguentum capsici. *Oleum amygdalae volatile purificatum*, volatile oil of bitter almonds (without hydrocyanic acid) becomes official; dose, $\frac{1}{4}$ to 1 minim, as a flavour for cod-liver and fish-liver oil emulsions.

On July 5, 1940, authority was given to use arachis oil in place of olive oil in making emplastrum plumbi, injectio hydrargyri (mercury cream), injectio hydrargyri subchloridi (calomel cream), and unguentum hydrargyri nitratis forte.

THE VITAMINS

Vitamin A (axerophthol)

This is formed by the hydrolysis in the liver of β -carotene; it has been isolated as pale yellow needles. The international unit is the vitamin A activity of 0.6 μ g (0.0006 mg.) of pure β -carotene and the daily requirements of the body are 75 to 100 units per kg. of body weight.

The chief functions of vitamin A are, in the young, to promote growth, and, later, to maintain the healthy structure and function of the protective epithelial tissues—skin and mucous membranes—and to regenerate the optic visual purple. It is of practical importance therefore both as a prophylactic and therapeutic agent in the retarded growth of children, in recurrent infections of the respiratory and alimentary tracts, and in nyctalopia. Clinically satisfactory results have been recorded in naso-pharyngeal catarrhs, tonsillitis, and periodontal diseases, as well as in a number of papular and pustular skin diseases; the claim that vitamin A accelerates granulation and epithelial growth when applied in a paraffin basis or as cod-liver oil to burns is not firmly established, although widely accepted. Night blindness is an early symptom of deficiency, but adequate supplies of vitamin A do not cure all forms of this disorder.

The liver fats of fish are rich in vitamin A. The Second Addendum to the British Pharmacopoeia, 1932, contains the following preparations:

Oleum Hippoglossi—Halibut-liver oil. 1 g. contains not less than 30,000 units of vitamin A with usually 2,500 to 3,500 units of vitamin D activity.

Dosage 0.06 to 0.3 c.cm., 1 to 5 minims.

Oleum Vitaminatum—Vitaminized oil. 1 g. contains 1,000 units of vitamin A and 100 units of vitamin D activity. It has been put forward as an alternative to cod-liver oil.

Dosage Prophylactic, 1 to 2 c.cm.; 15 to 30 minims, therapeutic, 3 to 6 c.cm.; 45 to 90 minims.

Emulsio Olei Vitaminati—An emulsion of which 50 per cent is vitaminized oil.

Dosage Prophylactic, 2 to 4 c.cm.; 30 to 60 minims; therapeutic, 6 to 12 c.cm., 90 to 180 minims.

Emulsio Malti cum Oleo Vitaminato—contains 15 per cent v/v of vitaminized oil.

Dosage 4 to 16 c.cm.; 60 to 240 minims.

Liquor Vitamini A Concentratus—1 g. contains 50,000 units of vitamin A activity.

Dosage 0.06 to 0.3 c.cm.; 1 to 5 minims.

Liquor Vitaminorum A et D Concentratus—1 g. contains 50,000 units of vitamin A and 5,000 units of vitamin D activity.

Dosage 0.06 to 0.3 c.cm.; 1 to 5 minims.

Proprietary preparations are avoleum, prepalin, essogen, planavit, and carotene.

Vitamin-B complex

This has now been divided into several factors of which the following are of medical interest.

Vitamin B₁ (Thiamine hydrochloride, aneurine hydrochloride)

This is a white crystalline powder of which 3 μ g (0.003 mg.) has the anti-neuritic activity of one international unit. The daily requirement in adults is at least 300 units.

Vitamin B₁ assists carbohydrate metabolism. Its pyrophosphoric ester is a catalyst promoting oxidation of pyruvic acid. If it be deficient, pyruvates and lactates are present in the blood, as in beri-beri; this defective glucose metabolism results in degeneration of the myelin sheaths of nerves.

Although vitamin B₁ improves growth, its main activity is antineuritic. It is prophylactic and curative for beri-beri, but the nervous symptoms may persist for months, it is effective also in the treatment of the peripheral neuritis of pregnancy, diabetes mellitus, and alcoholism, but is less reliable in improving post-diphtheritic paralysis. As bradycardia, and also anorexia, hypochlorhydria, and atony of the alimentary tract, especially of the colon, are symptoms of deficiency in animals, full doses of vitamin B₁ have acquired a clinical reputation as adjuvants in the treatment of cardiac failure with oedema, loss of appetite in debility, and atonic constipation. Thiamine hydrochloride is official in the Third Addendum to the British Pharmacopoeia 1932. The daily prophylactic dose is 0.3 to 0.6 mg, $\frac{1}{100}$ to $\frac{1}{160}$ grain, and the daily therapeutic dose is 0.6 to 1.8 mg, $\frac{1}{160}$ to $\frac{1}{40}$ grain. A warning is given that while solutions are stable if faintly acid, neutral and alkaline solutions deteriorate rapidly, especially in contact with air. The official adsorbate is pulvis vitamin B₁. Dosage (daily) prophylactic, 1 to 2 g (15 to 30 grains), being equivalent to 100 to 200 units, therapeutic, 2 to 6 g (30 to 90 grains) equivalent to 200 to 600 units. This is suitable for the treatment of moderate deficiency. Capsules and tablets containing usually 500 units of pure vitamin B₁ are also available. For beri-beri and neuritis, intramuscular or, if urgent, intravenous injections of the pure vitamin B₁, in a dosage of 2 to 10 mg (660 to 3,300 units) produce rapid improvement. Ampoules (benerva, berin, betaxan, collosol B₁, torulin, vibex) containing these doses are convenient for administration. The improvement from one injection may continue for some weeks.

Vitamin B₂ (Lactoflavin, riboflavin)

The phosphate of this yellow pigment, when conjugated with protein, forms a flavo-protein which acts as a 'respiratory enzyme' of the tissues, and probably facilitates the conveyance of hydrogen. The daily requirements are about 2 to 3 mg.

Vitamin B₂ appears to be essential for the maintenance of normal fat metabolism, but deficiency in animals causes cataract, cheilosis, and degenerative changes in the spinal cord and peripheral nerves. Clinical reports have not yet established a sphere of utility for lactoflavin although this is available for oral use as tablets containing 0.5 mg. and for subcutaneous or intramuscular injection as ampoules containing 0.5 and 1 mg.

Nicotinic Acid (Pellagra-preventing (P-P) factor)

Nicotinic acid, or its amide (nicotinamide), forms part of the enzyme, cozymase. This is the vitamin, or provitamin, which is deficient in pellagra. When given orally in a dosage of 0.5 to 1 g ($\frac{1}{2}$ to 15 grains) daily in divided doses, or 10 to 50 mg hypodermically, improvement follows in a few days in the dermatitis, stomatitis, diarrhoea, porphyrinuria, and nervous symptoms of the disease, complete cure may result within three weeks, although the neuritis may require vitamin B₁ in addition. Nicotinic acid also prevents and relieves porphyrinuria following sulphonamide therapy, and is available in tablets with sulphamylamide.

For the treatment of pellagra, tablets containing 50 mg. for oral use and ampoules for injection are obtainable.

Vitamin C (Ascorbic acid, cevitic acid)

Ascorbic acid is the antiscorbutic vitamin, and is a prophylactic and cure

for infantile and adult scurvy. One international unit represents the activity of 0.05 mg. of ascorbic acid; the adult daily requirement is about 500 units; reserves are stored in the adrenal cortex, liver, and kidneys, and the daily excretion in the urine averages 20 to 30 mg. daily.

Vitamin C regulates the cellular oxidation-reduction system and plays a part in the formation of red corpuscles, deficiency of it increases the fragility of the capillary walls, lowers resistance to acute infections, and may originate cataract. It has been recorded as of clinical value in the treatment of hypochromic anaemias, of capillary fragility in children, and of capillary haemorrhages in the skin and conjunctiva. In febrile states the requirements of the body for vitamin C are greater, and it is important to ensure that pregnant and nursing women, and children, receive adequate supplies of this vitamin, e.g., in the form of orange juice. Improvement in cases of incipient cataract have been reported from its administration.

Ascorbic acid is given orally. The daily prophylactic dose is 0.025 to 0.05 g. ($\frac{1}{4}$ to $\frac{1}{2}$ grain), equivalent to 500 to 1,000 units, and the daily therapeutic dose is 0.1 to 0.25 g. ($1\frac{1}{2}$ to 4 grains), equivalent to 2,000 to 5,000 units. It may also be given subcutaneously, intramuscularly, or intravenously, the dose, 50 to 100 mg., should be dissolved in 5 c.cm. of physiological saline and neutralized before use with half its weight of sodium bicarbonate. Ampoules containing 100 and 500 mg. are available for administration by injection.

Vitamin P

This is a flavone, probably hesperidin, which occurs with vitamin C in fruit juices. It is regarded as the factor which decreases capillary permeability and fragility. Hesperidin, in daily doses of 0.25 to 1 g. (4 to 15 grains) orally, or 10 to 50 mg. contained in ampoules intramuscularly, is at present on trial in the treatment of purpuras, particularly those of anaphylactoid, dietetic, and arsenical types.

Vitamin D

The natural vitamin D₃ is irradiated 7-dehydrocholesterol, the artificial vitamin D₂, or calciferol, is irradiated ergosterol. The international unit represents the activity of 1 mg. of a standard solution of irradiated ergosterol, equivalent to 0.025 μ g of calciferol. The daily requirements for adults are 500 units, for children 2,000 units, and for pregnant and lactating women 4,000 units.

The chief action of vitamin D is to lower intestinal alkalinity and so to lessen the formation of unabsorbable calcium soaps; it also aids phosphatase to deposit calcium phosphate in bones. Its deficiency produces rickets and imperfect calcification of the teeth, and, in pregnant and nursing women, osteomalacia. These conditions can be prevented and cured by adequate doses of vitamin D, the natural vitamin being more efficient than calciferol. Vitamin D also improves infantile tetany and spasmophilia, and diminishes the incidence of dental caries.

The preparations recently authorized for oral administration in the Second Addendum to the British Pharmacopoeia, 1932, are:

Emulsio Olei Morrhuae—An emulsion containing 50 per cent of cod-liver oil.

Dosage Prophylactic, 2 to 4 c.cm.; 30 to 60 minims (A, 1,000 to 2,000 units; D, 100 to 200 units); therapeutic, 6 to 12 c.cm., 90 to 180 minims (A, 3,000 to 6,000 units; D, 300 to 600 units).

Liquor Vitamin D Concentratus—1 g. contains 10,000 units of vitamin D.

Dosage 0.03 to 0.2 c.cm.; $\frac{1}{2}$ to 3 minims (D, 250 to 1,500 units).

Some preparations described under vitamin A contain also vitamin D.

Vitamin E

This is α -tocopherol, which is richly present in the oil from the embryos of cereals, e.g., wheat-germ oil. The dosage is 5 c.cm. (75 minims). The daily requirement of α -tocopherol is probably 2 mg., or, during pregnancy, 3 mg.

Deficiency of this vitamin causes in male animals permanent degenerative changes in the testicular germinal epithelium, and in female animals, although fertilization can occur, intra-uterine death and resorption or abortion of the foetus; this effect is temporary. It is believed that vitamin E acts either directly, or through the anterior pituitary, in increasing the formation of the corpus-luteum hormone, progesterone.

Vitamin E, in the form of wheat-germ oil, has proved successful in many cases of threatened and habitual abortion in women. Concentrates, obtained by removing the fatty acid glycerides, such as vitelol, germinol, and phytoferol, are usually prescribed in capsules containing 3 minims. Synthetic α -tocopherol acetate, 'ephynal', is also available in tablets of 3 mg. Bicknell records remarkable improvement in cases of muscular dystrophy, amyotrophic lateral sclerosis, tabes dorsalis, and amyotonia congenita from the use of wheat-germ oil.

Vitamin K (α -phylloquinone)

H. Dam of Copenhagen showed that haemorrhagic disease in chicks was due to lack of a fat-soluble vitamin present in alfalfa, kale, spinach, and other vegetables, but also obtainable from putrefying extracts of fish meal and casein. It can be formed by both enzyme and bacterial action, the latter accounting for its presence in the lower bowel even when absent from the diet, hence it is rarely deficient in man.

Vitamin K is essential in some unknown way to the formation of prothrombin. A deficiency of prothrombin may arise either from failure of absorption of vitamin K, or from the inability of the liver to utilize the vitamin. Intramuscular doses of vitamin K will raise the prothrombin content of blood to normal within 24 to 48 hours, but, if oral dosage is employed, it is usually necessary to give 5 to 10 grains of bile salts with each dose, otherwise this fat-soluble vitamin may not be absorbed. For oral administration, concentrates in oil containing 5 to 10 mg. are given in capsules, e.g. collosol K and klotogen. More satisfactory results are obtained from intramuscular injections of one of the synthetic methyl-naphthoquinones, for example, 2-methyl-1·4-naphthoquinone, which is available as kapilon and prokayvit in ampoules containing 5 mg. in oily solution; 10 mg. is given on the first day and 5 mg. daily till the prothrombin index is normal; the effect may last for three weeks.

Vitamin K has proved of value in accelerating coagulation time in the haemorrhagic diathesis due to deficient prothrombin which is associated with obstructive jaundice and sprue. It has also been successful in minimizing post-operative haemorrhage in jaundice and in preventing and treating neonatal haemorrhages. It does not influence haemophilia or purpura.

SEX HORMONES

Stilboestrol

The treatment of disorders of menstruation by oestrone, oestradiol, and oestradiol benzoate has been established for some years. Recently synthetic diethylstilbenes and their propionates have been shown to have similar actions and to be about twenty times more effective than oestrone when given orally.

Stilboestrol, neo-oestranol, or 4, 4' dihydroxy- α : β -diethylstilbene is given

orally in the form of tablets containing 1 mg. or 5 mg. daily; the latter quantity in some persons is liable to cause nausea and possibly vomiting about six or eight hours after the dose; 1 mg. thrice daily is the average dose. Stilboestrol may also be given intramuscularly in a dosage of 1 to 5 mg. in oily solution.

Stilboestrol dipropionate, 1 mg. in tablets for oral use or in 1 c.cm. ampoules for injection, has a more prolonged action and is less liable to excite nausea.

Hexoestrol, 4, 4'-dihydroxy- ζ , δ -diphenyl-*n*-hexane, 1 and 5 mg. in tablets for oral use and in 1 c.cm. ampoules for injection, is less active than stilboestrol, but is well tolerated.

These drugs have the same therapeutic applications as oestrone. In amenorrhoea, they are given during the oestrone fortnight of the menstrual cycle and withheld during the next fourteen days, at the end of which menstruation may occur; three such courses are usually given in the expectation of establishing regular periods. Similar principles are employed in treating dysmenorrhoea and sterility due to uterine hypoplasia, as well as menopausal vasomotor disorders. In the last, if menstruation has ceased, treatment may continue beyond a fortnight, the dosage being reduced as symptoms abate and stopped if it excites bleeding.

Stilboestrol, like oestrone, inhibits the action of the lactogenic hormone, prolactin, and, in mastodynia, dosage, confined to the five days preceding menstruation, usually gives relief; these drugs can also be used for the suppression of lactation. Vaginitis and pruritus vulvae are improved by treatment with stilboestrol.

The actions of stilboestrol may be supplemented by intramuscular or hypodermic injections of 1 to 2 units of progesterone, the corpus-luteum hormone, twice weekly during the second menstrual fortnight, to aid implantation of the ovum in treating habitual abortion; 2 to 10 units of progesterone daily may avert threatened abortion.

Prolactin

Prolactin, the lactogenic hormone of the anterior pituitary, is now available as physolactin for deep subcutaneous injection in the thigh; a course of treatment designed to initiate the secretion of milk consists of 5, 5, 2, 2, and 1 c.cm. on successive days.

Testosterone Propionate

Testosterone propionate has a greater and more prolonged effect than testosterone or androsterone, the male hormones, first isolated from the testes but now prepared synthetically.

Testosterone propionate may be given intramuscularly in doses of 50 mg. on alternate days, or tablets containing it may be implanted subcutaneously. The drug is on trial for prostatic hypertrophy which may be due to lack of male sex hormone. In women it inhibits the secretion of the anterior pituitary gonadotrophic hormone, prevents ripening of the ovarian follicle, and decreases menstruation. It has given relief from functional uterine haemorrhage and from mastodynia, but its therapeutic position is still uncertain.

SULPHONAMIDE COMPOUNDS

The full account of the actions and uses of the sulphonamides given in the previous volume needs but slight amplification. Recent experimental work indicates that the bactericidal action of these drugs lies in preventing the bacteria from utilizing *p*-amino-benzoic acid which is an essential for their growth.

It is recognized that the sulphonamides exert a local bactericidal action and are slowly absorbed from wounds: therefore a War Office Memorandum advises war wounds to be packed, as early as possible, with 5 to 15 grains of

sulphanilamide as a prophylactic. It is probable that sulphathiazole may prove a better local prophylactic than sulphanilamide.

During treatment with sulphanilamide a daily intake of fluid of from three to four pints should be ensured in order to prevent deposition of the acetyl derivative in the collecting tubules of the kidney; and, when toxic symptoms develop, a high fluid intake and diuretics hasten the excretion of the drug. Sulphonamides act rapidly, but to be effective they must be present in adequate concentration, namely about 10 mg. per 100 c.cm. in the blood, if oral administration fails to achieve this level, subcutaneous, intramuscular or, in urgent cases, intravenous, injections of the soluble preparations should be used. If no effect is apparent within ten days, it is recognized that further treatment with sulphanilamide is useless, but, if some benefit has been gained, a second course may be given after allowing an interval of three days.

The cyanosis which commonly arises during treatment is not due to anoxaemia, and does not call for reduction in dosage. It is also not explainable by the intracorporeal formation of methaemoglobin or sulphaemoglobin, as it may occur without any evidence of altered haemoglobin, it may be due to condensation products of the drug. The cyanosis is relieved by methylene blue, 0.1 to 0.2 c.cm. per kg. of body weight of a 1 per cent aqueous solution, or, more slowly, by 0.5 to 1 g. by mouth per day.

The principles for dosage with the sulphonamide compounds have become fairly uniform. During the first two days, the daily dose should be 1 g. per 20 lb. body weight in equally divided portions at four-hourly intervals, during the next two days, the total daily dose should be reduced by 1 g.; and for the remainder of the ten days' course a total of 3 g. daily should be given.

Sulphanilamide remains the standard preparation for most haemolytic streptococcal infections. It is effective in meningococcal, gonococcal, *Cl. welchii*, and *Bact. coli* infections, and is of some value in *Brucella abortus* infections, but not in pneumococcal, *Streptococcus viridans*, *St. faecalis*, or *Cl. oedematiens* infections.

Proseptasine (Benzylsulphanilamide)

This compound is not so soluble, is less easily absorbed and is therefore somewhat less efficient, but it is not so prone to cause toxic effects.

Soluseptasine

This is given intramuscularly, or, in urgent cases, intravenously, as it is relatively non-toxic. Since it is rapidly excreted, six doses per day of 20 to 30 c.cm. each may be required, hence it is useful only when oral dosage is ineffective in achieving an adequate concentration in the blood.

Albucid

This compound has a low toxicity, but seems also to have a much weaker bactericidal effect, certainly for the gonococcus; as this compound is not acetylated in the body, it was thought that it would be a more efficient urinary antiseptic.

Sulphanilamide ethyl-sulphonate, M.541, has also a low toxicity and feeble curative powers.

Rubiazol has an action similar to that of sulphanilamide but is rather better tolerated.

Sulphapyridine (M & B 693, Dagenan)

Sulphapyridine is undoubtedly superior in bactericidal powers to sulphanilamide in treating pneumococcal infections, and most authorities agree that

it is more efficacious in meningococcal and gonococcal infections; sulphapyridine also influences staphylococci, *Vibrio septique*, and some strains of *Str. viridans*. Unfortunately it is liable to cause nausea and vomiting which may, however, be obviated by giving it crushed in milk or in hot lemon juice.

Sulphapyridine soluble is given intramuscularly, 1 g. in 3 c.cm. ampoules, at four-hourly intervals, or intravenously, diluted with 20 c.cm. of physiological saline. As it is very alkaline, intramuscular injections, in order to obviate pain, should be deep, and care should be taken that none of the drug is allowed to escape into the subcutaneous tissues where it would cause necrosis.

Sulphathiazole (Thiazamide, M & B 760, 2-(*p*-aminobenzene-sulphonamido)-thiazole)

This compound is more soluble than sulphapyridine and therefore it is more rapidly and satisfactorily absorbed from the alimentary tract; it also causes less cyanosis, nausea, and vomiting, and has a somewhat lower toxicity.

The therapeutic position of sulphathiazole is at present very difficult to assess. Although it has bactericidal powers *in vitro* and *in vivo* against experimental pneumococcal, streptococcal, and staphylococcal infections, it does not appear likely that it will supplant sulphapyridine in the treatment of pneumonia, nor has it been found superior to sulphanilamide for streptococcal infections. Later clinical reports upon the treatment of staphylococcal infections have not substantiated the view that sulphathiazole might be much more effective in staphylococcal infections than sulphapyridine, different strains of staphylococci may be the reason for the variable results.

Severe staphylococcal infections arising from cellulitis did not respond well, except in a case of cellulitis due to *Staphylococcus aureus* with a negative blood-culture in which antitoxin was also used. Septicaemias from carbuncles (*Staph. aureus* and *Staph. aureus haemolyticus*) have recovered satisfactorily, and a proportion of patients with acute osteomyelitis have responded to treatment with sulphathiazole. There is evidence that, in combination with local surgical treatment of the lesions, sulphathiazole may have a value in the treatment of staphylococcal septicaemias, but its superiority over sulphapyridine is doubtful.

A derivative which crystallizes readily is excreted in the urine, hence, especially in febrile patients, a large fluid intake should be arranged.

Sulphamethylthiazole, 2-(*p*-aminobenzene-sulphamido)-4-methylthiazole, is said to have a much higher bactericidal action than sulphapyridine against *Staph. aureus*. Doses of 0.5 to 1 g. every four hours are advised, further clinical reports must be awaited.

Another active bactericidal substance, 4:4'-diamino-diphenyl sulphone, is slightly more effective against *Streptococcus viridans*, but causes more cyanosis, nausea, and vomiting than does sulphapyridine. Its diacetyl derivative, rodilope, has a low toxicity but, as the active substance is liberated slowly, it has not been satisfactory for acute infections.

Sulphapyridine in meningococcal meningitis

The War Office recently issued instructions for the immediate treatment of cases of meningococcal meningitis by sulphapyridine. In suspected or mild cases, whether the patient be conscious or unconscious, a first dose of 1 g. (3 c.cm.) of sulphapyridine soluble is given intramuscularly; subsequently, if the patient be unconscious, intramuscular injections of sulphapyridine soluble, 1 g., are repeated every four hours, but, if the patient is conscious and able to swallow, 1 g. of sulphapyridine in tablet form, or crushed and dissolved in 100 c.cm. of 1 per cent hot citric acid solution or hot lemon

juice, is given after the intramuscular injection, and then 2 g. by mouth four hours later.

In fulminating cases simultaneous injections of sulphapyridine soluble (a) of 1 g. (3 c.cm.) diluted in three or more volumes of physiological saline intravenously, and (b) of 1 g. (3 c.cm.) intramuscularly, are first given, a second dose, intramuscularly, is given four hours later. Because the alkalinity of sulphapyridine soluble may on injection cause pain and subcutaneous necrosis, it is recommended that a solution of procaine hydrochloride, 1 per cent, be injected while the needle is slowly pushed to its depth. Leaving the needle in position, the sulphapyridine is injected and, finally, more procaine solution is used to wash out the needle and to fill the needle track during withdrawal.

DRUGS ACTING ON THE HEART

Though powdered digitalis leaf and tincture of digitalis remain the standard preparations for treatment of auricular fibrillation and other cardiac disorders, increasing use is being made of digoxin, the crystalline glycoside from the leaves of *Digitalis lanata*.

Digoxin

When given orally in a single dose of 1 to 1.5 mg. or $\frac{1}{10}$ to $\frac{1}{10}$ grain, digoxin begins to slow the ventricle within one hour, the maximal effect develops in six hours and effects pass off in three days, the maintenance dosage is 0.5 mg. or $\frac{1}{40}$ grain, daily. In urgent cases intravenous administration of 0.5 mg. dissolved in 1 c.cm. of physiological saline will induce within a few minutes a beneficial effect which is fully developed within one or two hours.

Strophanthin

The use of strophanthin in a dosage of 0.25 to 1 mg. ($\frac{1}{40}$ to $\frac{1}{10}$ grain), or G-strophanthin (ouabain), which is about twice as powerful, by intramuscular or intravenous injection, in order to influence the heart within half an hour in urgent cases of auricular fibrillation, has declined in favour of the use of digoxin.

SEDATIVES AND HYPNOTICS

The introduction of pharmacopoeial and new proprietary names for important hypnotics should be noted, namely, bromethol for avertin, hexobarbitone soluble for evipan sodium, also known as cyclonal sodium and hexanastab, and phemitone for prominal.

Phemitone

Phemitone, N-methyl-5-phenyl-5-ethyl barbituric acid, has proved to be more effective than phenobarbitone in severe cases of epilepsy, it reduces the frequency of major seizures and, having a less hypnotic action, the patient's mental condition is better.

Sodium diphenylhydantoinate, epanutin, solantoin

In doses of 0.1 to 0.4 g. ($\frac{1}{10}$ to 6 grains) sodium diphenylhydantoinate also reduces the number and severity of epileptic fits, particularly in *grand mal*; it is also less hypnotic than phenobarbitone, but it has a small margin of safety. Toxic effects are ataxy, ptosis, mental confusion, dermatitis, and gingivitis.

DRUGS FOR TROPICAL DISEASES

Emetine

In the treatment of amoebic dysentery emetine hydrochloride is usually given hypodermically, in doses of 0.03 to 0.06 g., or $\frac{1}{2}$ to 1 grain, in 5 c.cm. physiological saline solution, thrice daily for ten days, or emetine bismuth iodide, 0.06 g., or 1 grain, orally, three times a day; the latter is usually more effective in treating dysenteric carriers. Chronic amoebic dysentery, which resists emetine, should be treated by acetarsol (stovarsol), 0.06 to 0.25 g., or 1 to 4 grains, in tablets by mouth, thrice daily during the weekly intervals in the emetine treatment, or by carbarsone, 0.25 g., or 4 grains, in gelatin capsules thrice daily for ten days; the latter is more toxic to the amoebae and safer for the patient. Enemas consisting of 200 c.cm. of 1 per cent carbarsone in 2 per cent. sodium bicarbonate solution may be given each evening, along with a soporific orally, until the enema has been retained by the bowel on five successive occasions.

Trypanosomicides

In trypanosomiasis, tryparsamide, antrypol, and suramin (germanin, Bayer 205) are chiefly employed, but recently the aromatic diamidines such as diamidino-stilbene, 4,4'-diamidino-diphenoxy-propane and also -pentane, have been shown by experiments *in vitro* and *in vivo* to be toxic to trypanosomes. Initial therapeutic trials in doses of 0.5 to 1 mg. per kg. of body weight intravenously, or 1 to 2 mg. per kg. intramuscularly, have given very rapid beneficial and hopeful results in trypanosomiasis, they are also being tried in leishmaniasis.

Stibophen

Stibophen is now the official name of foudadin or sodium antimony pyrocatechol disulphonate, which is used in schistosomiasis, granuloma inguinale, undulant fever, and oriental sore. It is given intragluteally as a 6.3 per cent solution. Three daily doses of 1.5 c.cm., 3.5 c.cm., and 5 c.cm. are usually given, then 5 c.cm. on alternate days, because it is slowly excreted and may give rise to nausea and vomiting as well as bradycardia, and even liver damage. The official dose (Third Addendum to the British Pharmacopoeia) is 0.1 to 0.3 g., $1\frac{1}{2}$ to 5 grains, by intravenous injection. It should not be allowed to come into contact with iron or its compounds.

Berberine sulphate

In oriental sore berberine sulphate in 2 per cent solution (orisol), injected weekly in doses of 2 or 3 c.cm. hypodermically around the oriental sore, is stated to be usually curative after three injections.

Mepacrine hydrochloride

The official name of mepacrine hydrochloride has been given to atebryn or quinacrine which is particularly toxic to the schizonts or asexual forms of the malarial parasite; the dosage is 0.1 g. ($1\frac{1}{2}$ grains) thrice daily for seven days. Pamaquin is the pharmacopoeial name for plasmaquine or praequine, the dosage is 0.01 to 0.015 g. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) thrice daily for four to seven days, and this drug is more effective on the gametocytes, or sexual forms, of the plasmodium. The former drug is frequently used with quinine for the acute attack, and followed by pamaquin to avert relapses.

HEPARIN

Heparin is derived from the mast cells of Ehrlich in the liver, it is a polysulphuric ester of mucoitin and is available as its calcium or sodium salt. Heparin is an active anticoagulant. The unit is the amount which will in the

could prevent clotting of 1 c.cm. of cat's blood for 24 hours; usually 1 mg. has 500 units of activity. The duration of the anticoagulant action increases with the dosage.

If added to drawn blood, 1 to 2 mg. of heparin per 100 c.cm. will delay coagulation for 30 to 45 minutes. As a substitute for citration, 20 mg. heparin (0.4 c.cm. of a 5 per cent solution) in 10 c.cm. of physiological saline for 500 c.cm. blood, is placed in the vessel in which the donor's blood is received.

If injected intravenously into a transfusion donor, its maximal action is reached within thirty minutes, declines after ninety minutes, and the coagulation time is again normal within two hours. An intravenous dose of 1 mg. per kg. body weight delays the coagulation time of blood, taken between 10 and 30 minutes after the injection, to about 40 minutes. For the injection, a 5 per cent sterile solution of heparin, containing 0.25 per cent tricresol, is used. The injections are devoid of risk.

Except when determining the Wassermann reaction, since heparin interacts with the blood complement, a syringe wet inside with a 1 per cent heparin solution may be used to prevent the clotting of blood prior to biochemical or cytological examination.

Heparin has also been used to prevent the extension of, and in treating, thrombosis. Doses of 75 to 100 mg., or more, have been given intravenously every four hours after surgical operations in order to avert anticipated thrombosis and to prevent the extension of venous thrombi. The drug is also under trial in cardiac cases, more particularly in infective endocarditis and in association with sulphapyridine treatment.

TETANUS TOXOID

To the officially recognized immunizing substances, there has been added tetanus toxoid, or *toxinum tetanicum detoxicatum*. This is a sterile filtrate of *Clostridium tetani*, detoxicated by treatment with formaldehyde (a solution) or by alum (a suspension in physiological saline). The dose subcutaneously or intramuscularly is 0.5 to 1 c.cm. or 8 to 15 minims. Tetanus toxoid is used to immunize those likely to be exposed, as a result of wounds, to the organism, when primary immunity is established small doses, even after two years, will greatly increase the amount of tetanus antitoxin circulating in the blood.

PART III
ABSTRACTS
OF MEDICAL LITERATURE

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also B.E.M.P., Vol. I, p. 1; Cumulative Supplement, Key Nos. 1-11; and Surveys and Abstracts 1939, p. 181.

Diagnostic Significance of Pain

Sensibility in the Abdomen

V. J. Kinsella, investigating problems of sensibility in the abdomen, operated on 40 cases of appendicitis under local anaesthesia, making observations on the sensitivity of various parts. Of these cases 22 were acute, with well-marked clinical tenderness, whereas 18 were 'interval' cases with little or no clinical tenderness. He confirmed the work of Lennander, finding that the anterior parietal peritoneum was invariably sensitive and that in most cases it accurately localized the stimulus. In 10 cases out of 19 in which the sensibility of the posterior parietal peritoneum of the right iliac fossa was investigated, it was found to be insensitive; in the other 9 cases its stimulation caused pain, referred in most cases to the right iliac fossa. The nerves of the mesentery were uniformly sensitive to physical stimuli, in most cases pain being referred to the middle line. In 17 cases the acutely inflamed, clinically tender appendix was directly squeezed, in 14 cases it was tender, but in 3 patients to whom morphine had been administered it was not definitely painful.

Kinsella, V. J. (1940) *Brit. J. Surg.*, **27**, 449

Lennander, K. G. (1902) *Mitt. Grenzgeb. Med. Chir.*, **10**, 38

— (1904) *Dtsch. Z. Chir.*, **73**, 297

ABORTION

See also B.E.M.P., Vol. I, p. 47, Cumulative Supplement, Key No. 12, and Surveys and Abstracts 1939, pp. 30 and 182.

Natural and Unintentional Abortion

Causes

Vitamin-C deficiency.—H. Hosemann and G. Athanasiu discussed whether hypovitaminosis-C or avitaminosis-C has a direct abortifacient action. They examined the vitamin-C content of the placenta and of the blood by means of the indophenol test. The placenta has a remarkable capacity for storing vitamin C, the content of which gradually increases during the course of a normal pregnancy. In the second to the fourth months of pregnancy the vitamin-C content is 2.9 mg. whereas at the end of pregnancy this rises to 4.77 mg. per cent. The blood shows a corresponding gradual diminution of the vitamin-C level. In patients who aborted, chemical examination of curetted placental fragments showed a much decreased amount of ascorbic acid and the authors therefore concluded that hypovitaminosis-C is a factor predisposing to abortion, its administration on the other hand being valuable in the prevention of abortion.

Incomplete Abortion

Diagnosis by vaginal smear examination.—P. I. Fletcher studied the value of the vaginal smear in the diagnosis of incomplete abortion. An outer basal or pavement cell zone appears in the vaginal mucosa in the post-partum period and after abortion. Daily smears were taken from the vaginas of all patients suspected of having an incomplete abortion. Twenty-four hours after operation the daily smears were resumed. They were also taken at regular intervals from pregnant patients and for two weeks post-partum. In some cases even later smears were

taken. Smears were also taken from normal persons at different stages of the menstrual cycle. Proliferative changes corresponding to the changes of the menstrual cycle were seen. In proved cases of incomplete abortion typical changes were found in the smears. Fletcher considered that the study of vaginal smears may form a valuable aid in the diagnosis of the condition.

Preventive Treatment

Vitamin E. C. G. Collins *et al.* investigated the use of wheat-germ oil, which is rich in vitamin E, in the treatment of 36 cases of spontaneous, threatened, or habitual abortion. The oil used was of the cold-pressed type. The daily maintenance dose ranged from 1 to 1½ fl. drachms, unless the patient began to show signs of threatened abortion, or had shown signs of threatened abortion when first seen. To this type of patient 8 to 12 fl. drachms were given during the first 24 hours, then 1 to 1½ fl. drachms daily. The oil was given until the patient reached 8 to 8½ calendar months of pregnancy. At the same time anterior pituitary-like hormone (antuitrin S) was given, in a dosage of 1 c.c.m. intramuscularly, each week until 4 to 4½ calendar months was reached. One rabbit unit of progesterone was given daily by the intramuscular route when cramp or bleeding was actually present. Dried thyroid, 1/10 to ½ gram, was given twice daily to all patients showing signs of hypothyroidism, such as obesity, irregular menstrual periods, slow pulse-rate, etc. Of 24 cases of threatened abortion so treated, 3 went to completion, 14 were delivered of normal, full-term children, and at the time of the report the remainder had continued the pregnancy without further signs or symptoms of abortion. Of 12 cases of habitual abortion, 8 had been delivered of normal, full-term healthy children, and another 4 were 6½ months pregnant.

Habitual Abortion

Vitamin-C therapy. H. Hosemann, investigating the vitamin-C content of the human placenta, found that, in a group of 11 women at full term, this was 4.7 mg per cent, whereas in 11 cases of spontaneous abortion and 2 of artificial abortion the average content was 2.9 per cent. It was also found that the vitamin-C content of the blood was higher in pregnant women at full term than in those whose pregnancies terminated between the second and fifth months. The author suggested that partial vitamin-C deficiency which upsets the normal oxidation-reduction potentials of tissues may interfere with the function of the corpus luteum, and consequently may be a contributory factor in the occurrence of spontaneous abortion.

Collins, C. G., Weed, J. C., and Collins, J. H. (1940) *Surg. Gynec. Obstet.*, **70**, 783.

Fletcher, P. F. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 562.

Hosemann, H. (1939) *Zbl. Gynak.*, **63**, 1784.

and Athanasu, G. (1939) *Zbl. Gynak.*, **63**, 1838.

Artificial and Intentional Abortion

Induction

Male sex-hormone. A. Binder employed a male sex hormone preparation, in sesame oil, intramuscularly in pregnant rabbits in an attempt to interrupt the pregnancies. In one group of rabbits injections were given daily for 5 days from the thirteenth day of pregnancy; a second group received injections for 4 days, from the twenty-first day; a third group from the eighteenth day; and a fourth group, which served as a control, was given injections of the solvent alone from the thirteenth day. The animals given the hormone aborted at various stages of pregnancy, whereas those given the solvent alone produced viable young. The author does not advise the application of this method to human subjects until further experimental work throws more light upon the biological effects of the hormone.

Binder, A. (1939) *Z. Geburtsh. Gynak.*, **119**, 285.

ABORTUS FEVER

See also B.E.M.P., Vol 1, p. 68, Cumulative Supplement, Key No 13, and Surveys and Abstracts 1939, p 183.

Aetiology*Raw Milk*

G. W. Elkington *et al* report 2 definite cases of mild undulant fever in a school of 400 boys, each of whom received daily a glass of raw ungraded milk. Twenty-six boys within a period of 3 to 7 weeks suffered from transient illness, generally characterized by mild fever, headache, malaise, and listlessness, and less often by abdominal pain, sore throat, sweating at night, insomnia, and a papular or urticarial rash. Ten of these 26 boys gave positive serum agglutinin reactions to *Br. abortus* in a titre of 1:20 to 1:1,100. Of 17 boys without symptoms of undulant fever, 5 had serum agglutinins to *Br. abortus* in titres of 1:20 to 1:1,100. *Br. abortus* was present in the raw milk supply. After a pasteurized supply was substituted for the raw milk, no more cases occurred after a further period of 3 weeks. It was concluded that the consumption of raw infected milk was followed by the occurrence of 2 definite cases of undulant fever, a number of subclinical cases, and 30 per cent latent infections among the boys, shown only by the agglutination test. A single negative agglutination in an individual may not have much significance, because a certain number of the patients never form agglutinins, and in others agglutinins do not appear for some days or even weeks after the attack. Attention is directed to the protean character of the infection, in the absence of agglutination tests the cases would have been diagnosed as sore throats, influenzal colds, gastro-enteritis, and other common infections. This seems to be the first recorded example of such an outbreak.

Elkington, G. W., Wilson, G. S., Taylor, J., and Fulton, F. (1940) *Brit. med. J.*, **1**, 477.

Treatment*Sulphapyridine*

G. S. Wilson and I. Maier reported experiments in which guinea-pigs infected with *Br. abortus* were given sulphapyridine by mouth or soluble sulphapyridine subcutaneously. These animals were compared with untreated control animals. At first the dosage of sulphapyridine by mouth was 1 to 1.5 mg. per gram of body weight, but this had to be reduced after a few days because of severe toxæmia in some cases. Even with a dosage of 0.6 to 0.8 mg. per gram a few deaths occurred. The dosage of soluble sulphapyridine given subcutaneously was at first 0.55 to 0.7 mg. per gram, but this also had to be reduced. Later it was abandoned altogether because of the occurrence of extensive local tissue necrosis, followed by dry gangrene of the extremities. Although the extent and severity of the lesions in the internal organs, the number of colonies growing from the sub-lumbar glands and spleen, and the serum-agglutinin titre were favourably affected by an average dose of 0.6 to 0.8 mg. per gram, given in 2 portions daily for a fortnight, complete sterility of the tissues was achieved only after maintaining this dosage for 4 to 6 weeks. Compared with the results obtained in previous experiments employing sulphanilamide, there appeared to be little to choose between the latter and sulphapyridine. The authors considered that, since abortus fever in man is a self-limited disease with a very low case mortality, the ordinary patient should probably not be exposed to the dangers associated with intensive sulphonamide treatment. Sulphonamide therapy should apparently be reserved for cases of abortus fever which have resisted other forms of treatment.

Wilson, G. S., and Maier, I. (1940) *Brit. med. J.*, **1**, 47.

ACCESSORY SINUSES OF THE NOSE

See also B F M P, Vol I, p. 77; and Surveys and Abstracts 1939, p. 183.

Congenital Occlusion of Nasal Choanae

P N Pastore and H L Williams reported 2 cases of congenital occlusion of the nasal choanae and reviewed 12 such cases. The condition results from faulty development, and the occlusion is usually of the bone. The patients do not usually suffer from respiratory embarrassment, but they often have auditory disturbances and other results of mouth-breathing. In the two reported cases the occlusion was bilateral in one and unilateral in the other. Both were successfully treated surgically. Of the 12 cases reviewed, 5 were males and 7 females. The occlusion was completely bony in 8 of the cases. In only 4 of the cases was the occlusion bilateral.

Pastore, P N, and Williams, H L (1939) *Proc. Mayo Clin*, **14**, 625.

Chronic Hyperplastic Sinusitis*Bacteriology*

R C Grove and J B Larrion made bacteriological observations on 200 operative cases of chronic hyperplastic sinusitis, examining 365 washings from the maxillary and sphenoidal sinuses, 130 polypi and membranes removed from the ethmoidal and sphenoidal sinuses, and 108 membranes from the maxillary sinuses. Of these patients 165 had asthma, 25 hay fever, 12 vasomotor rhinitis, and 7 urticaria or angioneurotic oedema. In one-fourth of the patients there were two or more allergic manifestations. It was found that 88 per cent of all washings, 80 per cent of the ethmoidal and sphenoidal membranes, and 96 per cent of the antral membranes showed bacterial growth. In cultures of both washings and membranes staphylococci predominated. Haemolytic streptococci were found twice as often in the antral membranes as in the washings or in the ethmoidal and sphenoidal membranes. Pneumococci and *S. aureus* were present much more often in the washings and in the ethmoidal and sphenoidal membranes than in the antral membranes. The high percentage of haemolytic streptococci in the antral membranes indicates its importance as an agent of infection which may often be overlooked. The fact that only 4 per cent of the antral membranes appeared to be sterile shows the importance of sinus membranes as a focus of infection.

Grove, R C, and Larrion, J. B (1940) *J. Allergy*, **11**, 271.

Treatment*Short-wave Therapy*

W P I Paterson reports the results of short-wave therapy in 126 acute and subacute cases of sinus infection during 3 years. Of these, 96 were improved, the results in 22 were doubtful, and 8 did not show any improvement or even deteriorated. Short-wave therapy increases the circulation and dilatation of the capillaries, and probably thus exerts the therapeutic effect. No changes in intranasal temperature were noted. Tuberculosis, heart failure, and malignant growths contra-indicated its use. Carelessness may cause burns, for the collection of perspiration under the electrodes is prone to have this result. Blood pressure is lowered and occasionally accompanied by dizziness. All deviations of the septum and spurs should be cleared up first, and complete drainage is the first essential. In allergic or polypoidal conditions, discouraging results were noted. Ten to 15 minutes is generally the duration of each treatment. The treatment is ideal for sinusitis in the majority of children, 10 or 12 treatments are usually sufficient. It is very important that the patient's only reaction to treatment by short waves should be a sensation of pleasant and comfortable warmth. Undue heat or intensive aching of the head or face during treatment is certain evidence that the current volume is excessive. Short-wave energy conversion to heat seems to be cumulative hence all administration of short-wave therapy should begin with mild, even approaching ultra-conservative, dosage.

A. R. Hollender also discusses short-wave therapy in nasal sinusitis. Short-wave diathermy differs from other methods of application of external heat in that it can penetrate and heat bone, it is erroneous to suppose that short-wave therapy exerts any action other than heat on the tissues. Heat acts on the diseased sinuses by inducing hyperaemia, a flow of discharge, and, if used long enough oedema, it is also analgesic. The treatment can be used even in the acute stages, but drainage should be established at the proper time in all cases. Short-wave therapy alone is not as a rule sufficient, and to obtain adequate results should be combined with other appropriate measures. The treatment usually shortens the course of the disease, but it is useless in chronic sinusitis which has failed to respond to other therapy. The author investigated the local changes of temperature in the tissues induced by short-wave therapy in 20 patients with acute exacerbations of maxillary sinusitis. The highest rise of temperature was 1.5°F , and in 6 cases the temperature actually fell. Eighteen cases of acute maxillary sinusitis were treated with short waves alone, a control group was treated by other routine measures, and in a third group the two treatments were combined. The least successful results were obtained in the first group, and the most successful in the third. Of 14 cases of chronic maxillary sinusitis, 7 cases were treated with short waves alone, and 7 with short waves combined with other forms of routine treatment. Only one case in the first group showed any improvement, whereas 3 in the second gave some favourable response.

X-ray Therapy

W. B. Frior and C. A. Waters, reporting on the use of X-irradiation in several patients with infection of nasal sinuses, claim excellent results after 4 bi-weekly doses of 100 r each, measured in air. It is sometimes necessary to use 600 r for 3 weeks in order to obtain the best possible results. This dosage was delivered at 125 kv., 5 ma., 35 cm. focal skin distance and with filtration of 4 mm. aluminium. The prevention of epilation is provided by covering the hair, eyebrows and eye-lashes with strips of lead, in children the dental buds in the maxilla being similarly protected. The authors report cures, i.e. the complete disappearance of symptoms and clarification of sinuses, in 34 per cent of cases. In 38 per cent there was marked improvement, shown by complete or almost complete disappearance of symptoms, but with a slight remaining opacity of the sinuses as determined by subsequent radiography. In 13 per cent of cases there was moderate improvement, i.e., symptoms returned after a few weeks or months. In 15 per cent of cases there was no improvement. Only certain types of sinus disease are amenable to irradiation, allergic cases are unlikely to respond to the irradiation unless there is associated infection. Lymphoid hyperplasia in the nasopharynx in children associated with thickened sinus membranes is of great significance to the radiologist, as these cases do very well under irradiation.

I. T. Catewood examined 22 cases of chronic sinusitis, roentgenologically and rhinologically, before and after they had received X-ray therapy. They found no definite evidence of uniform improvement of the infection. With the exception of one case, microscopical examination of the polypoid content of 8 antrums which had had X-ray therapy showed no obvious difference from similar pathological contents of other antrums which had not received this treatment.

Catewood, I. T. (1940) *Arch. Otolaryng.*, Chicago, **31**, 275.

Frior, W. B., and Waters, C. A. (1939) *Amer. J. Roentgenol.*, **42**, 857.

Hollender, A. R. (1939) *Arch. Otolaryng.*, Chicago, **30**, 749.

Paterson, W. P. L. (1940) *Canad. med. Ass. J.*, **42**, 454.

ACHALASIA

See also B.E.M.P., Vol. I, p. 116, Cumulative Supplement, Key No. 18, and Surveys and Abstracts 1939, pp. 43 and 185.

In the Alimentary Tract

Of the Cardiac Sphincter

Associated with oesophageal ulcer.—N. L. Fekchoff records the rare combination

of achalasia of the cardia with oesophageal ulcer. The patient, a woman of 63, was admitted to hospital for abdominal pain and vomiting; the pain was in the left hypochondrium, and radiated through the back, and down the left side to the leg. It began during a meal, and was relieved by vomiting or by alkalis. It occurred in attacks lasting 3 days, with intervals of freedom of 4 to 5 months. Her appetite was good, but she was afraid to eat. Radiologically there was extreme dilatation with elongation of the oesophagus. A diagnosis of achalasia of the cardia was made, and surgical treatment was instituted. Four years later an attack of violent vomiting occurred, followed some weeks later by haematemesis. X-rays indicated ulceration near the lower end of the oesophagus.

Treatment with nitrites—M. Ritvo and I. I. McDonald state that the administration of amyl nitrite or nitroglycerin produces a disappearance of the stenosis of the oesophagus in many cases of cardiospasm, permitting the passage of fluid and food into the stomach. Abolition of the obstruction gives the patient relief from his distressing symptoms, permits accurate X-ray visualization of the oesophagus and the remainder of the gastro-intestinal tract, and may facilitate the passage of dilators and thus lessen the dangers of traumatism or perforation during instrumentation. After the inhalation of amyl nitrite, the effect is generally almost immediate, the oesophageal obstruction beginning to disappear in from 30 seconds to 4 or 5 minutes. The dosage of nitroglycerin is $\frac{1}{100}$ gr., the tablet being allowed to dissolve under the tongue. The effects of the drugs are of short duration. Nevertheless, these agents appear to have a definite, though limited, application in the treatment of cardiospasm.

Cardiospasm

P. P. Vinson defines spasm of the cardia as constant spastic contraction of the cardiac opening of the oesophagus without organic stenosis and with more or less dilatation of the gullet above the point of obstruction; the clinical syndrome of which consists of epigastric pain and regurgitation. "Achalasia" is given among the synonyms, but there is not any discussion of Hurst's view that so-called cardiospasm is in reality achalasia (failure to relax) of the cardia. In the treatment of cardiospasm, very few drugs are of value. Hypodermic injection of morphine is sometimes necessary for pain, and so is atropine, or belladonna orally. But the safest, simplest and best method is to introduce dilators through the mouth, guided into the stomach by a twisted silk thread swallowed previously; anaesthesia is not necessary. Since 1925 the author has treated more than 450 patients by preliminary dilatation with a 60 French sound followed by Russell's hydrostatic dilator.

Treatment

Special anaesthesia—L. D. Telford and H. T. Simmons stated that, if the sympathetic nervous system overacts in the control of a sphincter, or if the parasympathetic nervous system under-acts, the sphincter cannot relax, and dilatation and hypertrophy occurs above it. This is the mechanism of production of congenital megacolon and of cardiospasm. They reported 7 cases of the former condition and one of the latter which were treated by spinal anaesthesia alone with excellent results. The case of cardiospasm has remained completely cured. Decicain was used to induce the anaesthesia, and it is necessary for it to reach as high as the anterior root of the sixth thoracic nerve in order to paralyse the whole of the sympathetic supply to the gut. The suggested explanation of its action in these conditions is that the temporary complete block of the sympathetic system allows, on its recovery, the two halves of the autonomic system to act in unison once more.

Plummer-Vinson Syndrome

P. P. Vinson, under the title 'hysterical dysphagia' (the Plummer-Vinson syndrome), states that, though in his first series of 69 cases there were 12 men, he now does not believe that it occurs in males, and that the 12 cases in males were examples of a distinct disorder, functional dysphagia, which occurs in both sexes and usually results from psychological shock in the emotionally unstable who chew their food thoroughly for 10 to 15 minutes at a time. A satisfactory radiological examination of these patients is almost impossible because they cannot swallow any kind of mixture opaque to X-rays. Diagnosis must be made from the history of the

symptoms alone. Oesophageal instrumentation causes great discomfort and increases rather than diminishes the intensity of the dysphagia. In the treatment of this functional dysphagia drugs should be avoided, the patient's confidence should be secured, and he should be re-educated in swallowing by being encouraged, when alone with the medical attendant, to swallow a dry piece of bread or a sandwich without the help of water.

Eckhoff, N. L. (1939) *Guy's Hosp. Rep.*, **89**, 267.

Ritvo, M., and McDonald, L. J. (1940) *Amer. J. Roentgenol.*, **43**, 500.

Telford, I. D., and Simmons, H. T. (1939) *Brit. med. J.*, **2**, 1224.

Vinson, P. P. (1940) *The Diagnosis and Treatment of Diseases of the Esophagus*, pp. 85 and 136, Springfield, Ill.

ACHONDROPLASIA

See also B.E.M.P. Vol. I, p. 135, and Cumulative Supplement, Key No. 20.

Aetiology

Role of Advancing Maternal Age

A. Bleyer discussed the role of advancing maternal age in the causation of achondroplasia. In 303 cases of achondroplasia he found that 6.6 per cent were born to mothers between the ages of 15 and 19 years, 19.8 per cent to those between 20 and 24 years, 28.3 per cent between 25 and 29 years, 24.09 per cent between 30 and 34 years, 14.19 per cent between 35 and 39 years, and 5.94 per cent between 40 and 44 years. Comparison between these figures and the number of normal children born to women in these age groups shows that the chance of giving birth to an achondroplastic child begins soon after the reproductive period and increases steadily to its end. The incidence of the production of this congenital abnormality therefore tallies with that of mongolism in its relation to the age of the mother.

Bleyer, A. (1939) *Amer. J. Dis. Child.*, **58**, 994.

ACNE

See also B.E.M.P., Vol. I, p. 156, Cumulative Supplement, Key No. 23; and Surveys and Abstracts 1939, p. 185.

Acne Vulgaris

Aetiology

Effect of iodine—It has been thought that iodides and bromides tend to cause exacerbations of acne, as well as to produce acneiform eruptions. I. F. Traub and R. Emmet report the blood iodine content of 58 patients, 45 with acne vulgaris and 13 with miscellaneous dermatoses. The values for 22 normal subjects served as controls. In the control group of patients, whose blood iodine was apparently normal, the average value was approximately 6 micrograms per 100 c.c.m. The average iodine content of the patients with acne vulgaris was 5.975 micrograms, which was approximately within the normal range. The values for males averaged 5.3 micrograms per 100 c.c.m. and those for females 6.65 micrograms. The failure to find a higher blood iodine in patients with acne vulgaris than in 'normal' persons possibly indicates that the part, if any, played by iodine may be qualitative, or that the iodine may, in patients with this disease, be stored in the cutaneous tissues.

Treatment

Vitamin C.—M. Lozza combined the use of vitamin C and calcium in the treatment of 25 cases of juvenile acne. In one group of patients 20 drops of a 5 per cent solution of ascorbic acid were given by mouth and 25 mg. of ascorbic acid in 2 c.c.m. of a 10 per cent solution of calcium gluconate injected intramuscularly each day.

In another group 40 to 50 mg. of ascorbic acid in 5 to 10 c.cm. of a 10 per cent solution of calcium gluconate were injected intravenously each day. In practically all cases there was a marked improvement; after a month's treatment the skin appeared to be much healthier, and there was a diminished secretion of sebum and sweat, and a gradual disappearance of the acne. The patients also gained in weight.

Vitamin D—C. A. Simpson *et al.* investigated the effect of massive doses of vitamin D in a series of 22 patients with acne. The dosage employed was 5,000 to 20,000 U.S.P. units of vitamin D daily in the form of viosterol in oil, or 25,000 U.S.P. units of vitamin D and 30,000 U.S.P. units of vitamin A in capsules, 1 to 2 capsules being given daily (U.S.P. units are equivalent to I.U.). Of the 22 patients treated 10 (45 per cent) showed some improvement, but in only a few cases was the therapeutic result permanent. Ten per cent of the patients became worse during treatment, and the others remained about the same. In no case did the results obtained compare with those from irradiation. The authors concluded that vitamin D alone, or combined with vitamin A, was of no practical value.

Insulin—H. C. Semon and F. Herrmann report the results of an investigation of the blood-sugar tolerance curves of 11 patients with acne. In 7 of the 8 female and in 2 of the 3 male patients there was a lag as compared with the normal curve, thus indicating delay in sugar assimilation. Of the younger females, 5 showed exaggeration of the lag at the onset of menstruation, and in the other 3 the shift of the curve to the right was more pronounced both inter-menstrually and at the end of the period. These results suggested a trial of insulin, and, in the 7 women with a lowered sugar-tolerance, it was injected for at least 5 to 7 days before the period fell due, and during the first half of the period. In 2 patients 5 units were injected twice daily; in the other 5, once daily at first, and later 8 to 10 units 2 or 3 times per week. In 5 of the 7 female patients on inter-menstrual series of injections, 8 units per dose was given. Of these, a girl aged 17, and a woman aged 40, were injected twice weekly for 3 months. In 2 other patients, aged 21 and 24 respectively, insulin was injected thrice weekly, beginning in each case 2 weeks after the period had begun. Of the 3 men, 2 were given insulin twice weekly, 5 units and 8 units respectively. In all 9 cases the results, without local treatment of any kind, were consistently encouraging, and 4 of them had not relapsed 5 to 8 months after cessation of the injections. All the female patients in whom acne had previously resisted both local and other treatments were markedly benefited, the lesions undergoing involution during the injections, not only in the inter-menstrual period, but even just before the onset, when the symptoms had previously been aggravated. The males were much benefited, more so than by the local measures previously applied for years.

Lozza, M. (1939) *Minerva medica*, 2, 235.

Semon, H. C., and Herrmann, F. (1940) *Brit. J. Derm.*, 52, 123.

Simpson, C. A., Ellis, F. A., and Kirby-Smith, H. (1940) *Arch. Derm. Syph., N.Y.*, 41, 835.

Hraub, L. F., and Emmet, R. (1940) *Arch. Derm. Syph., N.Y.*, 41, 506.

ACROMEGALY

See also B.E.M.P., Vol. I, p. 166, and Cumulative Supplement, Key No. 24.

Clinical Picture

Association with Diabetes Mellitus

C. Coggeshall and H. F. Root investigated 29 patients with both acromegaly and diabetes mellitus. The average interval between the onset of the two conditions was 9.2 years. In 20 per cent of the cases diabetes mellitus occurred in other members of the family. In 127 acromegals not known to have diabetes mellitus 2 per cent were found to be diabetic. The type of obesity found in diabetes mellitus

was seen in 73 per cent of 113 acromegalics. Necropsy showed that splanchnomegaly occurred only in the presence of acromegaly in those who had suffered from acromegaly, diabetes mellitus, combined acromegaly and diabetes mellitus, and Simmonds's syndrome. It is, however, possible that pituitary over-activity produced the diabetes mellitus in other cases, but did not last long enough to produce splanchnomegaly. In 50 necropsies on cases of diabetes mellitus no variations in size of other organs, comparable to the size of the pancreas, were found. In 4 cases of acromegaly due to mixed tumours of the pituitary, diabetes occurred. Diabetes mellitus associated with acromegaly did not differ in any way from other cases of diabetes mellitus. These patients are liable to the same complications as ordinary diabetes. Chronic diabetes mellitus can be produced experimentally in dogs by the injection of large amounts of crude anterior pituitary extract from the cow. The authors suggested that such a diabetogenic hormone might be used to study the condition in man.

Coggeshall, C. J. and Root, H. I. (1940) *Endocrinology*, **26**, 1.

ACTINOMYCOSIS

See also B. F. M. P., Vol. I, p. 173, Cumulative Supplement, Key No. 26, and Surveys and Abstracts 1939, p. 186.

Mycology

More than 100 species of the actinomycetes, more or less pathogenic to man, have been recorded. Knowledge of the disease and the organism has been chiefly limited to the *Actinomyces bovis* of Hartz (*A. bovis* of Wolff and Isaac). G. C. H. Franklin reports a case of actinomycosis of the lower jaw, the organism from which, after many months of bacteriological investigation, could not be correlated with any known species. It was claimed as a new species, under the name *Actinomyces moormanii*. Like *A. grammis*, it probably occurs in the mouth as a saprophyte. The cultural procedures employed in its identification are fully described.

Franklin, G. C. H. (1940) *Ann. intern. Med.* **13**, 1205.

Clinical Picture

Generalized Actinomycosis with Prominent Spinal Symptoms

G. J. Dixon reported a case of generalized actinomycosis occurring in a man of 27 years. The patient had lower abdominal pain for 4 weeks accompanied by a remitting fever. This improved and he returned to work but 2 months later developed pain over the right hip. A cold abscess appeared in the right loin, it was incised and healed, but then broke down again. About 12 days later he became much worse. The temperature was high, left-sided pleurisy followed by empyema developed, and the thoracic spine became painful and rigid. Aspiration of the empyema revealed pus containing sulphur granules. The patient went down-hill and died 6 weeks later. During this time the spine became increasingly and abnormally mobile. Necropsy showed that the disease probably began in the appendix. It had spread to involve the fascia around the lower thoracic and upper lumbar vertebrae. The twelfth thoracic vertebra which contained an abscess cavity was completely collapsed and there was also an abscess in the second lumbar. The right transversus abdominis and left psoas muscles were necrosed.

Lacrimal Concretions

A. Hagedoorn describes lacrimal concretions caused by actinomycetes, they may occur in either the superior or the inferior canaliculus. In both canaliculi a swelling ultimately appears and yellow pus can be expressed from the puncture. When the infection occurs in the lower canaliculus the obstruction produces epiphora. Slitting the canaliculus exposes clumps of soft yellowish material, not adherent to the wall, which block the lumen. Hagedoorn describes a method for obtaining a pure culture of the actinomycetes for diagnosis.

Dixon, G. J. (1939) *Brit. med. J.*, **2**, 686.

Hagedoorn, A. (1940) *Arch. Ophthalm.*, N.Y., **23**, 689.

Treatment

H. S. Morton considers that pure infections of actinomycosis respond better than mixed infections to drugs, and that possibly the various strains of actinomyces react differently to the same drug. In most cases surgical treatment is imperative and, if at all possible, complete excision should be carried out. The prognosis varies enormously with the site affected. In all suspected cases early search for the ray fungus should be carried out, and the abscess wall cultured when the pus is sterile.

Sulphanilamide

M. R. MacCharles and J. W. Kippen report the success of treatment by sulphanilamide supplementing surgical drainage of 3 cases of suppurative actinomycotic lesions, in the antrum, the mandible, and the neck. The diagnosis depended on the recognition of the organism in the pus, which in one case contained staphylococci.

MacCharles, M. R., and Kippen, J. W. (1939) *Canad. med. Ass. J.*, **41**, 490.
Morton, H. S. (1940) *Canad. med. Ass. J.*, **42**, 231.

ACTINOTHERAPY

See also B. I. M. P., Vol. I, p. 180, Cumulative Supplement, Key No. 27; and Surveys and Abstracts 1939, p. 187.

Filtered Ultra-Violet Rays

In Surgery

H. Paschoud recommends the use of filtered ultra-violet rays in surgical treatment. Ultra-violet rays have their greater photochemical activity between 2500 Å and 2950 Å, and an erythema followed by pigmentation is caused by rays of these wave-lengths. These wave-lengths seem to have a certain affinity for the skin and mucous membrane, whilst more deeply-lying tissues might require other wave-lengths. Other important photochemical manifestations are caused by rays of those wave-lengths, such as an antirachitic action (2500-3000 Å), and transformation of ergosterol to vitamin D (2700-2850 Å) and of histidine to histamine (2300 Å). The rays under 2600 Å are dangerous to living tissue, as rays of 2500 Å coagulate albumin. In view of the use of ultra-violet rays for the irradiation of wounds and internal organs, it is very necessary to use only filtered rays of a defined wave-length to prevent dangerous burns. Especially useful for those purposes is the American Window Westinghouse lamp. It is possible to irradiate with this lamp for long periods (20 minutes and longer) with erythema doses.

Paschoud, H. (1940) *Pr. méd.*, **48**, 438.

Irradiation of Air in Wards

Prevention of Respiratory Infections

I. H. Barenberg *et al.* studied the effect of irradiation of the air in a ward on the incidence of infections of the respiratory tract. A group of infants of from 7 to 16 months of age were placed in a ward the air of which was irradiated intermittently, one half-hour on and one half-hour off, from 6 a. m. till 8 p. m. daily, for a period of 4½ months. A similar group of children were observed during the same period in a ward the air of which was not irradiated. A definite decrease in the incidence and severity of infections was noted among the children in the irradiated ward, as compared with those in the non-irradiated ward.

Barenberg, I. H., Greene, D., and Greenspan, L. (1940) *Amer. J. Dis. Child.*, **59**, 1219.

Sterilization of Air in Operating Rooms

C. J. Kraissl *et al.* stated that the unsterile air in the operating room is an important source of wound contamination. This can be practically eliminated by the use of

ultra-violet irradiation, in the proper spectrum, with an intensity that will not injure animal tissue exposed for the time of a usual operation. When employing ultra-violet irradiation for reducing air contamination in operating rooms, surgeons are cautioned to determine that the quality of the radiation is in the most efficient part of the spectrum, and that the intensity is great enough to render the air relatively sterile, and yet not so great that it will injure tissue for the period of time it will be exposed.

Kraussl, C. J., Cimioti, J. G., and Meloney, I. L. (1940) *Ann. Surg.*, **111**, 161

Ultra-Violet Irradiation

Delayed Tanning Brought Out by Blood Transfusion

F. O. Jodar reported the case of a boy aged 9½ months who had received an intramuscular injection of whole blood and two kinds of iron tonic, for the treatment of anaemia. He had also had 18 weekly treatments with a mercury-vapour lamp. His haemoglobin and red blood-cell counts still being low, he was given 180 c.cm. of citrated blood intravenously. This was followed by a moderate reaction 2 hours later. The next day the child's skin appeared yellow, and this pigmentation was found to be a tanning, corresponding to the area exposed to the ultra-violet light. Jodar concluded that the child's cells had been sensitized to ultra-violet light, but at the time of the treatment the precursors of pigment (tyrosine and phenylalanine) had been absent from his blood. When they were supplied by the transfusion from a normal person, tanning quickly followed.

Dangers

A. C. Cipollaro described the harmful effects which may follow exposure to ultra-violet irradiation. The most common undesirable reaction is erythema solare, or sunburn. Some hypersensitive individuals may develop a papular, vesicular, and erythematous eruption with considerable pruritus. Others may develop lesions of the lips resembling herpes simplex. Urticarial lesions may occur, some lesions may be capped with vesicles or bullae. Sensitization to ultra-violet light may be increased by the parenteral or oral use of such photosensitizing drugs as acriflavine, barbiturates, fluorescein, gold sodium thiosulphate, sulphonamides, and haematoporphyrin. The application of eosin, oil of bergamot, crude coal-tar, and liquor carbonis detergens to the skin before exposure to ultra-violet light markedly accentuates the local effect. Some persons with desquamating fungous diseases, such as tinea versicolor, when exposed to ultra-violet light, develop a peculiar mottled tan. Psoriasis may occasionally become generalized after over-exposure to ultra-violet light. Some patients with the discoid type of lupus erythematosus, exposed to ultra-violet light long enough to produce erythema, may develop a wide-spread dissemination of the disease. There is experimental and clinical evidence that ultra-violet rays are carcinogenic.

Cipollaro, A. C. (1940) *Arch. phys. Ther.*, **21**, 223

Jodar, F. O. (1939) *Amer. J. Dis. Child.*, **58**, 1047

ADENOIDS

See also B.E.M.P., Vol. I, p. 193, and Surveys and Abstracts 1939, p. 187.

Diagnosis

Radiography

G. T. Calthrop described a radiological method of diagnosing adenoids in children. A soft ray should be used so as to show up details of the soft tissue. With the chin raised, a true lateral view of the skull is taken. The central ray must pass 1 inch below, and 1 inch in front of, the external auditory meatus. In the presence of adenoids, though not of small remnants left after operation, an opaque mass is seen in the nasopharynx.

Calthrop, G. T. (1940) *Lancet*, **1**, 1005.

ADIPOSIITY

See also B E M P., Vol. I, p. 202; and Surveys and Abstracts 1939, p. 188

Clinical Picture

Macrogenitosomia Praecox in one Twin

H Gardiner-Hill and J S Richardson record the case of one of 2 male twins with macrogenitosomia praecox without any demonstrable morbid lesion. This boy, aged 8½ years when admitted to St. Thomas's Hospital in January, 1939, was alive when the report was written. The possible causes of this condition were fully discussed, such as a pineal tumour, cerebral lesions other than pineal growth, tumours of the adrenal cortex, interstitial-cell tumours of the testes. There was not any family history of the condition, a reference being made to 3 cases in one family and 5 other examples in 4 generations in the same family recorded by Rush *et al.* This appears to be the first recorded case in a twin.

Gardiner-Hill H., and Richardson, J S. (1939) *St Thom Hosp Rep*, 2nd ser. **4**, 35.

Rush, H. P., Bilderback, J. B., Slocum, D., and Rogers, A. (1937) *Endokrinologie*, **21**, 404.

Genito-Pituitary Adiposity (Frohlich's Syndrome)

Pituitary Function

H Schwarz *et al.* investigated the pituitary function in cases of adiposo-genital dystrophy. The rise in blood ketones produced in the rat by the injection of sera from cases of the disease revealed a tendency toward a greater increase in these ketones than was produced by the sera of normal children, this appeared to indicate a tendency toward a greater concentration of ketogenic hormone. The degree of ketonaemia following a high-fat test meal may be higher than, or decrease to the same degree as, in normals. Both normal children and those with the disease respond essentially in the same way to the administration of insulin, adrenaline, and to the Staub-Traugott effect. Present methods have not shown demonstrable amounts of gonadotrophic principle either in the sera of normal children or in those with the disease. The administration of anterior-pituitary-like gonadotrophic hormone to 3 children, though producing gonadal development, did not affect the obesity.

Schwarz, H., Newman, A. B., and Baum, H. (1940) *Endocrinology*, **26**, 605.

Treatment

Benzedrine Sulphate

G Rosenthal and H A. Solomon treated 22 obese patients with benzedrine sulphate. The daily dose ranged from 10 to 30 mg. taken in one to three doses. The diet was reduced but any thyroid the patient had been having was stopped. In 5 patients the effect of the drug alone was tried, and in 5 others the effect of withdrawing the drug for a time was investigated. It was found that the weight lost was regained if the drug were stopped for one to two weeks. Benzedrine sulphate caused loss of weight in this series, in some instances producing loss of appetite by reducing the gastric tone. The action of benzedrine in reducing weight is not known, but it is probably due to a diuretic effect.

Rosenthal, G., and Solomon, H A. (1940) *Endocrinology*, **26**, 807.

ADRENAL GLAND DISEASES

See also B.F M P., Vol. I, p. 232; Cumulative Supplement. Key No. 30; and Surveys and Abstracts 1939, pp. 109, 166 and 189.

Physiology

Presence of Orally Active Medullotrophic Principle in Extract of Pituitary

J. B. Collip records observations strongly suggesting that the anterior pituitary

contains a hormone with a specific trophic effect upon the so-called 'dark-cells' of the adrenal medulla. The author had previously become convinced that a certain pituitary extract had an effect when administered orally. This seemed to be confirmed by clinical tests by some of the author's associates. The tentative hypothesis was advanced that the clinical effects might possibly be explained by stimulation of the adrenal cortex, particularly as the extracts used contained some corticotrophic hormone, as shown by injections into hypophysectomized rats. The gland material employed was an 83 per cent alcoholic extract of prime pituitary tissue quickly prepared and concentrated and kept at low temperatures. Feeding as well as injection experiments were again undertaken with the purpose of determining its action, if any, on the adrenals of hypophysectomized rats. An adrenal medullary reaction ensued, characterized by great enlargement of the 'dark-cells'.

Previously it had been believed that only the adrenal cortex was controlled by the pituitary, though Anselmino, Herold, and Hoffmann had claimed that an anterior pituitary principle controlled the medulla, but the changes they described in the cells of the adrenal medulla—heavy vacuolation—differed from those in Collip's animals.

Collip, J. B. (1940) *Canad. med. Ass. J.*, **42**, 2.

Anselmino, K. J., Herold, L., and Hoffmann, E. (1934) *Klin. Wschr.*, **11**, 1724.

Addison's Disease

Clinical Picture

Associated with diabetes mellitus.—A. L. Bloomfield described a case in which diabetes mellitus and Addison's disease were coexistent. The Addison's disease which supervened on a pre-existent diabetes showed no proof that it was due to tuberculosis of the adrenal gland or to the presence of a tumour. It was found that, as this latter condition progressed, the patient's insulin requirement, formerly in the neighbourhood of 40 units a day, fell to between 4 and 6 units. Injections of desoxycorticosterone acetate 5 mg., increasing to 25 mg., not only failed to produce a more marked glycosuria, but actually lowered the blood sugar. Tscham, a non-synthetic cortical extract given in doses of 30 c.cm. over 3 or 4 days, had a completely contrary effect. Its action was similar to that of cortical extract injected into animals whose pancreas and adrenal glands had been removed.

Course

Duration.—L. G. Rowntree reports 3 cases of 'clinical' Addison's diseases with survival for more than 15 years, thus showing the longest survival time in 116 cases discussed in the book by Rowntree and A. M. Snell (1931). One patient survived for 18 years and died with generalized tuberculosis, the adrenals being tuberculous. A second patient with mild Addison's disease due to tuberculosis or syphilis, one or both, is alive after 15 years, and in the third patient, also living, the disease, idiopathic in origin and probably functional in character, has been almost completely latent for 12 years, and therefore represents arrest of symptoms starting 17 years ago. These cases are published to indicate the actual survival of the occasionally mild cases under older methods of treatment (the Murhead regime and adrenaline).

Treatment

R. M. Wilder of the Mayo Clinic, where so much research work on this disease has been carried out, reviews the great progress since 1930 when Swingle and Pfiffner and others provided active extracts of the adrenal cortex, and shows the great debt that clinical medicine owes to biochemical workers. Before 1930 the majority of patients died in a few months, and none could stand unusual stress of any kind. These extracts were weak and very expensive and the results were disappointing, as shown by A. M. Snell's report in 1934 that 7 only of 46 patients were alive more than a year after the extracts were given. In 1933 R. F. Loeb and others found that salt exerted a beneficial influence on the disease, and soon afterwards it was shown experimentally that after adrenalectomy dogs excreted more sodium than chloride, and accordingly a mixture of sodium citrate with sodium

chloride was given in a solution, 'Addison's elixir', containing 10 g. of the chloride and 5 g. of the citrate of sodium for a dose. In 1936 Allers, Nilson, and Kendall showed the adverse effect of potassium on the disease, a daily intake of 4 g., which was no larger than that in an ordinary diet, produced an excessive excretion of sodium and precipitated symptoms of a crisis unless the patient was taking the cortical extract. Treatment by additional salt and sodium citrate and reduction of potassium to 2 g., was successful, and in July, 1937, Ryncarson, Snell, and Hausner reported that 24 out of 43 patients who were treated between 1933 and 1937 were alive. The results remained as good or were better until early in 1939 when the synthetic crystalline preparation, desoxycorticosterone, was introduced at the Clinic. Up to that date there had not been any fatal case among the 30 of Addison's disease for a year. Elevation of the blood pressure above the normal almost never resulted from the sodium treatment or from moderate doses of the cortical extract. But after treatment with desoxycorticosterone acetate the blood pressure rose to hypertensive levels and oedema was noticed in spite of cessation of the sodium citrate and reduction of the sodium chloride dosage. There were 7 deaths among patients taking desoxycorticosterone, and these did not resemble the deaths from crisis formerly seen in Addison's disease. It became clear that desoxycorticosterone acetate not only obviated the need for much additional sodium but even made it dangerous. Light was thrown on the action of desoxycorticosterone acetate by the case of a patient doing well on that drug who was given a provocative test, used to determine the presence of insufficiency of the adrenal cortex, namely rigid restriction of sodium and chloride and the administration of potassium, a positive result being a prompt excessive excretion of sodium and symptoms of an Addisonian crisis. In this patient the test was quite negative. This encouraged the suspicion that more potassium might be given to patients taking desoxycorticosterone acetate, and later it was shown that the disturbing influence of that drug could be controlled by suitable adjustment, at a higher level, of the intake of potassium (Fooke, Power, and Kepler). Now sodium citrate is not prescribed, and very little ordinary salt is given. What is still needed is an inexpensive and readily available synthetic product which possesses not only the salt and water activity of desoxycorticosterone acetate, but a carbohydrate activity comparable to that of Kendall's Compound E.

Desoxycorticosterone acetate—T. B. Fooke, Jr., *et al.* describe the experience at the Mayo Clinic of the treatment of Addison's disease by desoxycorticosterone acetate. At first, and in 3 patients, desoxycorticosterone acetate was given in the same way as the ordinary cortical hormone as regards a liberal amount of sodium chloride (10 to 12 g.) and additional sodium in the form of the citrate (usually 5 g.), and restriction of potassium (2 to 3 g.). This method was very unsatisfactory and caused retention of salt and water and sometimes massive oedema. The treatment by desoxycorticosterone was continued, but the administration of sodium and potassium was reversed, namely, on the same lines as the provocative test for insufficiency of the adrenal cortex, introduced by Cutler *et al.*—restriction of sodium chloride and the liberal administration of potassium citrate daily. This method was most successful. When desoxycorticosterone acetate is given, the low potassium diet and extra sodium are not recommended. The relative merits of the treatment of Addison's disease by desoxycorticosterone acetate as compared with other preparations and the ultimate merits of the use of a liberal intake of potassium in conjunction with desoxycorticosterone acetate are regarded as problems for future solution.

W. O. Thompson, *et al.*, find that oral administration of extracts of the adrenal cortex in glycerin solution has some effect on patients with Addison's disease, but that by this route it is less than one-fifth as effective as when injected hypodermically. As commercial extracts of the adrenal cortex, given in the usual doses to cases of Addison's disease, have in general been extremely disappointing, R. F. Loeb *et al.* tested on 13 patients with Addison's disease the effects of esters of the synthetic desoxycorticosterone of Reichstein. The most striking results were the retention of water and salt and decrease in the concentration of potassium in the serum; and serum calcium concentration decreases with the administration of the remedy. There were not any effects on carbohydrate metabolism, pigmentation, or the excretion of riboflavin. In all the 13 patients the arterial blood-pressure reached the normal in the course of 2 to 4 weeks; in 2 cases it rose gradually to 160/92 and

146/108 mm. Hg. respectively. Overdoses of desoxycorticosterone caused in 10 out of the 13 patients oedema of the face and ankles varying from mild and transient to massive anasarca (oedema of adrenal origin). As recent experiments have shown a similar action of desoxycorticosterone and progesterone, their effects were compared on 3 cases of Addison's disease, but progesterone was without effect on Addison's disease.

Subcutaneous implantation of desoxycorticosterone.—W. M. Firor employed subcutaneous implantation of pellets of synthetic adrenal cortical hormone in 17 patients with Addison's disease. The rate of absorption from each pellet of desoxycorticosterone acetate, weighing between 100 and 125 mg., was 0.3 mg. per day. Pellets were inserted into the subcutaneous fat. The pellets were found to meet the patients' requirements for cortical hormone for periods ranging from 4 to 9 months. All but 2 of the 17 patients returned to full activity, and were able to work as strenuously as before their illness began. The average gain in weight was 5.4 kilos. The improvement in systolic and diastolic blood-pressure was uniform. All the patients maintained a positive sodium and chloride balance, and kept normal concentrations of potassium, sodium, and chloride ions in the blood plasma.

Allers, W. D., Nilson, H. W., and Kendall, I. C. (1936) *Proc. Mayo Clin.*, **11**, 283.

Bloomfield, A. L. (1939) *Johns Hopk. Hosp. Bull.*, **65**, 456.

Cutler, H. H., Power, M. H., and Wilder, R. M. (1938) *J. Amer. med. Ass.*, **111**, 117.

Firor, W. M. (1940) *Ann. Surg.*, **111**, 942.

Loeb, R. F., Atchley, D. W., Benedict, L. M., and Ieland, J. (1933) *J. exp. Med.*, **57**, 775.

— Ferrabee, J. W., and Rogan, C. (1939) *Trans. Ass. Amer. Phys.*, **54**, 285.

Reichstein, T., and Luw, J. von (1938) *Helv. chim. Acta*, **21**, 1197.

Rowntree, L. G. (1939) *Trans. Coll. Phys., Phila.*, 4th ser. **7**, 261.

Ryncarson, E. H., Snell, A. M., and Hausner, I. (1938) *J. clin. Med.*, **134**, 11.

Snell, A. M. (1934) *Int. Clin.*, **3**, 46.

Steiger, M., and Reichstein, T. (1937) *Helv. chim. Acta*, **20**, 1164.

Thompson, W. O. Jr., Thompson, P. K., Taylor, S. G., and Hoffman, W. S. (1939) *Trans. Ass. Amer. Phys.*, **54**, 277.

Tooke, T. B., Jr., Power, M. H., and Kepler, I. J. (1940) *Proc. Mayo Clin.*, **15**, 365.

Wilder, R. M. (1940) *Proc. Mayo Clin.*, **15**, 273.

Hyperfunction of the Adrenal Cortex: Hyperplasia and Neoplasm

Diagnosis of Adrenal Tumours

Modified air injection, X-ray technique.—Employing the method, described some years ago, of facilitating the radiological definition of adrenal tumours by the injection of air into the perirenal space before the X-ray examination, O. Cope and R. Schatzki report the results of 163 injections of air in 78 patients suspected of having adrenal tumours. In 15 patients diagnosed by means of this technique as having adrenal growths, this finding was confirmed by operation, and in 2 other patients by necropsy. This method of diagnosis is particularly valuable in making it possible to diagnose and remove adrenal tumours earlier than otherwise would be done, and thus it should lower the mortality. Attention is directed to some points of importance in the technique; the injection of air is made through the triangular pad of fat below the kidney, and should be done slowly and under very low pressure, so as to avoid fat-embolism and puncture of an adrenaline-forming tumour of the adrenal medulla, which, from flooding the circulation with adrenaline, may cause grave symptoms and even sudden death. Puncture of the kidney or adrenal gland may be followed by haemorrhage and a haematoma, and care is necessary to prevent such an accident.

Clinical Picture

Pseudo-hermaphroditism.—I. D. Miller and P. J. Kenny reported a case of adrenal

cortical hyperplasia associated with pseudo-hermaphroditism. The patient, 10 years old, had the outward appearance of a male. Pubic and axillary hair appeared at 4 years, the external genitals began to develop and rapidly became of adult size, and the voice changed to that of a man. He had had to shave from the age of 7. At no time was the real sex suspected. He was not then considered to be a hermaphrodite, but to have a moderate degree of hypospadias. There was apparently complete cryptorchidism. There was no evidence of any male gonad. Complete female organs were found in the pelvis. A small vagina, just large enough to admit a No. 12 rubber catheter, was found, and communicated with the urethra which opened on to the perineum. The patient died 36 hours after operation. Post-mortem examination showed a unilateral adrenal hyperplasia with complete absence of the other adrenal gland.

Masculinization Associated with an Adrenal Cortical Tumour of the Ovary

J. T. Bauer reports the case of a negress, aged 32, with masculinization associated with a large irregular tumour of the left ovary, 14 by 13 by 5 cm., the cells of which were large and resembled those of the adrenal cortex, and partially retained fuchsin with Vines' stain. The tumour was regarded as an ovarian hypernephroma or hypernephroid, and not as derived from lutein cells. The adrenals were small, and the cortex did not give a positive reaction with Vines' fuchsin reaction, but the partial retention of fuchsin by the tumour cells suggests a close relation of the neoplastic cells and the androgenic tissue found in patients with the adreno-genital syndrome. There were 23 litres of cloudy yellow-green fluid with a specific gravity of 1.020. There were not any metastases. The patient died shortly after laparotomy. Preliminary examination showed that the cells in the anterior lobe suggested a male rather than a female arrangement, but a further report will be made.

Bauer, J. T. (1939) *Bull. Amer. Clin. Lab., Phila.*, **3**, 259.

Cope, O., and Schatzki, R. (1939) *Arch. intern. Med.*, **64**, 1222.

Miller, I. D., and Kenny, P. J. (1940) *Brit. J. Surg.*, **27**, 760.

AGRANULOCYTOSIS

See also B. I. M. P., Vol. I, p. 261, Cumulative Supplement, Key No. 32, and Surveys and Abstracts 1939, pp. 177 and 193.

Aetiology

Gold Therapy

G. S. Minck reports a case of total agranulocytosis after gold therapy in a woman, aged 22, who was treated with a short course of parenteral gold sodium thiosulphate for arthritis. The percentage of polymorphonuclears and basophils fell to 0, and the number of granulocytes to 0. She made a complete recovery. Seventeen other recorded cases of pure agranulocytosis after gold therapy were collected, and it was estimated that this complication occurs in about 1 case in every 1,000 treated with gold salts. Fifty per cent of the reported cases proved fatal. A bad prognostic sign was a fall in granulocytes below 30 per c.mm. Eosinophilia was a good sign, all cases with more than 8 per cent recovering, even though complete agranulocytosis followed. Age, sex, disease, dosage of gold, or gold salt employed, and length of time between beginning of therapy and onset of agranulocytosis appeared to make no difference to the prognosis.

Sulphapyridine Therapy

B. Pringle *et al.* reported a case of agranulocytosis following sulphapyridine therapy. In 6 days 22.5 g. of the drug had been given for lobar pneumonia. On the tenth day the temperature, which had fallen to below normal on the fifth day of the disease, rose, and by next day had reached 102° F. Treatment with sulphapyridine, in a daily dosage of 2.5 g., was recommenced. On the seventeenth day the dosage of sulphapyridine was reduced to 1.5 g. daily, and on the twenty fifth day the drug was stopped, a total dosage of 46.5 g. having been given. A blood count then

revealed under 200 white cells per c.mm., with a complete agranulocytosis. The red cells were 2,340,000 per c.mm. and the haemoglobin 45 per cent. Blood transfusion and pentnucleotide were given. The patient made a good recovery.

Mirick, G. S. (1940) *Amer. Rev. Tuberc.*, **41**, 344.

Pringle, B., Dockeray, G. C., and Mitchell, R. H. (1940) *Brit. med. J.*, **1**, 212.

ALCOHOLISM

See also B.E.M.P., Vol. 1, p. 280, Cumulative Supplement, Key No. 36, and Surveys and Abstracts 1939, p. 194.

Toxic Effects

Psychological Effects

G. H. Stevenson states that there are 2 types of problem drinker, the first being generally well-built, attractive and friendly, but indolent, undependable, and selfish, and the second and smaller group, generally slight or small in stature, tense, nervous, moody, ambitious, and hard-working. Treatment is by no means easy, and relapses are frequent. Addiction to alcohol should be regarded as a special type of psychoneurosis, and calls for psychotherapy. The problem drinker may not require hospitalization, unless he is verging on delirium tremens, is physically depleted, or obsessed by a compulsion to drink. Diet should be varied, ample, and rich in vitamins and carbohydrates. Psychotherapeutic conversations should comprise about 3 one-hour periods weekly for about a year. The following types of alcoholic addicts should not be accepted for treatment: those who do not want to be well; alcoholic psychopaths whose psychopathy has shown itself since childhood by constant failure to adjust; generally associated with other types of behaviour disorder, such as swindling or chronic immorality, manic-depressives, in the manic phase of whom the immoderate use of alcohol is not an uncommon symptom; and mental deficiency associated with alcoholism. Thorough and persistent psychotherapy gives a much better prognosis than has previously been recognized.

Acute Alcoholism

Treatment with vitamin B₁ in delirium tremens.—H. I. Kiene *et al.* employed the following technique with good results in 5 cases of delirium tremens. Every 3 hours, 4 ounces of bonded rye whisky was given, in order to prove that the intake of alcohol was not responsible for the delirium tremens. Synthetic crystalline vitamin B₁ was given intravenously in a dosage of 50 mg. or more in 24 hours. A dietary containing an average of 200 I.U. of vitamin B₁ daily was given, and supplementary vitamin B₁ in the form of yeast and vitamin capsules was also given in some cases. In 5 control cases no whisky or intravenous vitamin B₁ were given. The same dietary was given. In the patients receiving vitamin B₁ there was an almost immediate improvement in the physical and mental condition. The generalized dehydration and roughness of the skin noted cleared up within 24 to 36 hours. The hallucinations and fear reactions also rapidly decreased and generally disappeared within 36 hours. The average recovery period was 2.4 days. In the control cases, the average recovery period was 4.2 days.

Treatment with glucose and insulin.—W. Goldfarb *et al.* investigated the effect of glucose and insulin on the rate of disappearance of alcohol from the blood of intoxicated patients. It was found that the injection of 15 units of insulin alone had no effect on the blood alcohol, whereas the injection of 50 c.cm. of 50 per cent glucose solution intravenously caused a moderately increased fall in blood alcohol only in severely intoxicated patients. In less severely intoxicated patients there was no change. On the other hand the administration of 50 c.cm. of 50 per cent glucose solution and 15 units of insulin accelerated the decrease in blood alcohol in all patients; a reduction of blood alcohol ranging from 75 to 275 mg. per 100 c.cm. occurred within 2 hours.

Treatment with nicotinic acid.—F. Mainzer and M. Krause state that alcoholic polyneuritis had been found to be due to a deficiency of vitamin B arising in the

condition. They reported a case of delirium tremens occurring in a chronic whisky addict which did not respond to intensive vitamin-B₁ therapy, but was cured in 12 hours on giving 0.6 g. of nicotinic acid by mouth in two doses of 0.5 and 0.1 g. The delirium was associated with gastro-intestinal symptoms and stomatitis, both of which disappeared with the treatment.

In a child—H. M. Taylor and A. R. Cross reported a case of acute alcoholism in a child of 3½, following the swallowing of a ½-pint of ethyl alcohol (70 per cent). All the indications were that this case would have been fatal. The child, who soon passed into coma, was treated by gastric lavage, about 150 c.cm. of tap water being left in the stomach. About an hour later he was given 200 c.cm. of strong coffee by stomach tube, and 150 c.cm. of 10 per cent glucose intravenously. As he did not respond, he was admitted to hospital, where he was given 150 c.cm. of 10 per cent glucose intravenously, and 10 units of insulin intramuscularly. He responded somewhat to this treatment, and recovered consciousness. He was next given 0.5 c.cm. coramine (nikethamide) intramuscularly. He then made an uneventful recovery.

Chronic Alcoholism

Diagnosis in surgical patients—A. King Foster investigated the problem of concealed chronic alcoholism in surgical patients. He stated that, though acute alcoholism was easily recognized, the chronic form was often difficult. The diagnosis should be made from a history taken from the patient and his relatives, from the clinical examination, and from laboratory tests. Many signs and symptoms of chronic alcoholism are cited including tremor of the tongue and facial muscles, disorientation, and hoarseness. He reported 8 cases of surgical conditions complicated by chronic alcoholism in which the patients were abnormal or unmanageable until they were allowed some alcohol. The condition might arise in any man who has taken any form of alcohol regularly, and in those who have become inebriated more than 3 times in their life. Concealed chronic alcoholism was rare before 18 and after 75 years of age. The mental and emotional make-up of the patient should be assessed in diagnosis, and sedatives and vitamins, both pre- and post-operatively, are useful in treatment.

Foster, A. K. (1939) *Arch. Surg., Chicago*, **39**, 57.

Goldfarb, W., Bowman, K. M., and Parker, S. (1939) *J. clin. Invest.*, **18**, 581.

Kiene, H. I., Streitwieser, R. J., and Miller, H. (1940) *J. Amer. med. Ass.*, **114**, 2191.

Mainzer, I., and Krause, M. (1939) *Brit. med. J.*, **2**, 331.

Stevenson, G. H. (1940) *Canad. med. Ass. J.*, **42**, 57.

Taylor, H. M., and Cross, A. R. (1940) *J. Pediat.*, **16**, 341.

Treatment of the Alcoholic

Establishment of a Conditioned Reflex

W. L. Voegtlin described a new physiological approach to the treatment of alcoholism by inducing a conditioned reflex aversion to alcohol. The treatment is safe, having a mortality of less than 0.15 per cent, and should result in about 64 per cent of permanent cures. Younger people and women are less promising patients than mature men, from the viewpoint of ultimate cure. The basis of the method is that certain nauseant drugs are used to elicit the unconditioned reflex of nausea and vomiting; the sight, smell, and taste of alcoholic beverages serve as the conditioned stimulus, and thus a conditioned reflex can be established. A distaste is thus created for the conditioned stimulus, amounting to a strong and definite aversion to the sight, smell, and taste of liquor. The technique of treatment is as follows. The patient is made comfortable in the treatment room, then 6 to 12 minims of a mixture consisting of emetine hydrochloride, 50 grains, pilocarpine nitrate, 25 grains, ephedrine sulphate, 23 grains, and water to 40 c.cm., is given hypodermically. The emetine nausea begins in 2 to 8 minutes. A few seconds before its onset, alcoholic liquor should be given, and following the onset of nausea, all types of liquor should be forced on the patient, making certain that he smells deeply each glass. Warm water is given frequently to afford easy emesis and to avoid itching. After emesis is completed, the above routine is repeated.

until the nauseant effect has begun to wane. Occasionally a small dose of apomorphine hydrochloride ($\frac{1}{10}$ gr) in conjunction with the emetine is necessary to cause emesis. About 5 to 7 seances are generally necessary--with rest periods between--over about 5 days.

Vogtlin, W. L. (1940) *Amer J med Sci*, **199**, 802.

ALKALOSIS

See also B I M P, Vol. I, p. 292, Cumulative Supplement, Key No. 37, and Surveys and Abstracts 1939, p. 198.

Morbid Anatomy

Renal Changes

B. M. Nicol discussed the renal changes which may occur in alkalosis. In alkalosis the patients are often dehydrated. They suffer from lassitude, depression or irritability, headache, anorexia, and drowsiness. Latent or manifest tetany and coma may occur. Various renal manifestations such as deposits of calcium in the kidneys and blood and casts in the urine have been found. The majority of the kidney damage occurs in the tubules. The author observed 7 cases. 4 cases of pyloric stenosis complicated by alkalosis, and 3 cases of pyloric stenosis in which it was experimentally produced. In the second group dehydration did not occur. Albumin and casts only appeared in the urine of dehydrated patients. Their urine was also always acid in spite of the presence of alkalaemia. Nicol therefore concluded that these observations confirmed the suggestion that the renal symptoms are due to the dehydration impairing the blood supply to the kidneys. He thought the urine was acid because the damaged renal tubules failed to secrete alkaline radicles and are therefore instrumental in maintaining the alkalaemia.

Nicol, B. M. (1940) *Quart J Med*, **9**, 91.

Clinical Picture

Cerebrospinal Fluid

H. Agar and I. Macpherson report 2 cases of severe alkalosis in which the cerebrospinal fluid showed a diminished chloride content and an increase in urea. Similar observations were made on normal subjects and patients with various diseases; the cerebrospinal fluid showed the same changes in intestinal obstruction, severe vomiting, and Addison's disease.

Agar, H., and Macpherson, I. (1940) *Lancet*, **1**, 171.

ALLERGY

See also B I M P, Vol. I, p. 302, Cumulative Supplement, Key Nos. 40-52, and Surveys and Abstracts 1939, p. 198.

Aetiology

Role of Water Balance

R. A. Kern suggested that changes in the water balance of the body may influence the occurrence of allergic phenomena; that water and salt retention favour the development of allergic reactions; that dehydration and salt loss antagonize allergic reactions; that increased intake of sodium, by tending to increase interstitial fluid and oedema, also favours the development of allergic reactions; and that increased intake of potassium, or decreased intake of sodium, by tending to increase intracellular fluid and to decrease interstitial fluid and oedema, will antagonize allergic reactions. Such shifts in water balance occur clinically in many conditions, or they may be induced by a number of therapeutic measures. The

effect of hydration and dehydration on allergic reactions is purely non-specific. Therefore the causes of changes in water balance have not in themselves any aetiological significance with regard to allergy.

Insulin

H. Ulrich *et al.* reported a case of allergic reaction to insulin in a non-diabetic man of 53, who received insulin for the purpose of gaining weight. About 7 years previously he had received a course of insulin for the same purpose. Nine days after beginning this second course of treatment, large itching urticarial patches appeared on the arms and wrists, spreading next day over the entire body. The insulin was stopped and the urticarial patches gradually faded. Since the insulin employed had been prepared from pork pancreas, an injection of 5 units of insulin made from beef pancreas was tried. Shortly after this the patient had a severe chill, a temperature of 101 F., recurrence of generalized urticaria, and severe substernal pressure and pain. The blood pressure fell to 80/60 mm. Hg. Four months later crystalline zinc-insulin was tried, and similar allergic reactions occurred. Skin test with extracts of pork and beef muscle, solutions of crystalline zinc-insulin, and solutions of glycerin and tricesol were made, but all, except those made with insulin, gave negative results. Rapid desensitization was effected by giving intradermally small amounts of insulin, beginning with 0.01 c.c.m. (0.4 units) and working up to 0.05 c.c.m. in the course of 8 hours, then continuing with 0.02 c.c.m. subcutaneously and working up to 0.2 c.c.m. within four hours. Thus within 14 hours, in 13 injections, the dosage had been raised from 0.01 c.c.m. (0.4 units) to 0.2 c.c.m. (8 units). Thereafter the patient was able to take 5 units, 3 times a day, without further allergic symptoms.

Karaya (Indian) Gum

K. D. Figley reported 16 cases of hypersensitivity to karaya (Indian) gum. The substance is used in wave-setting preparations and certain laxatives. Hand lotions, tooth-pastes, fillings of pies, ice-cream, and salad dressings may also contain it. Seven of the 16 patients had often ingested the gum. Its particles may also be inhaled, for example, after a wave-setting lotion had dried. It may produce in the hypersensitive hay-fever, asthma, dermatitis, or gastro-intestinal discomfort.

Hypersensitiveness to the Bee and Mosquito

Diagnosis. R. L. Benson describes the lesions which appear in those who are hypersensitive to the sting of the bee and mosquito, and shows that individuals can be desensitized against these stings. Following the bite a wheal first appears, but 24 to 48 hours later a large, red, hot, painful swelling which lasts for several days is formed. A specific reaction, similar to that of the insect's bite, was obtained in susceptible persons upon intracutaneous injection of extracts of the body tissues of the insect. These extracts were specific for the group of insects concerned and were water-soluble, non-dialysable, and thermostable. Repeated injections of this antigen produce a general desensitization. Remoculation locally prevents the lesion due to the antigen from progressing beyond the wheal stage. Passive transfer by the Prausnitz-Kustner technique could be obtained for the immediate reaction only in the bee, and imperfectly in the mosquito.

Relation to Hyperplastic Disease of the Respiratory Tract

N. Fox *et al.* describe the relation of borderline allergy to hyperplastic disease of the respiratory tract. Neither the texture, the colour of the tissues, nor the character of the exudate gives any hint of the allergic nature of the borderline condition, since pallor, oedema, and eosinophilia are usually absent. The diagnosis of borderline allergy of the respiratory tract is made by finding gross hyperplastic changes in a patient with a history, or a family history, of allergy, and in whom sensitivity to particular allergens is found. In many persons with hyperplasia there is good evidence of allergy in the following conditions: chronic intermittent nasal obstruction, chronic lymphoid pharyngitis, frequent colds, recurrent acute laryngitis,

pachydermia laryngis, singer's nodes and papillomas, chronic purulent discharge from the nose in children, and tubo-tympanic catarrh.

Benson, R. L. (1939) *Arch. intern. Med.*, **64**, 1306.

Figley, K. D. (1940) *J. Amer. med. Ass.*, **114**, 747

Fox, N., Harned, J. W., and Peluse, S. (1940) *Arch. Otolaryng., Chicago*, **31**, 502.

Kern, R. A. (1940) *Amer. J. med. Sci.*, **199**, 778.

Ulrich, H., Hooker, S. B., and Smith, H. H. (1939) *New Engl. J. Med.*, **221**, 522.

Asthma and Hay-Fever

Treatment

Artificial pyrexia.—R. W. Hyde used fever therapy in 32 cases of allergy which had not responded to simpler methods of treatment. No attempt was made to distinguish the different aetiological factors in the cases of asthma and hay-fever treated. All the treatments consisted of a temperature raised to not more than 103° F., and for not longer than one hour. In most cases the temperature was raised to 102° F. in 25 minutes, with immediate termination of treatment, allowing the temperature to fall gradually to normal. All fevers were induced in a humidified external-heating type of cabinet. Abundant fluids in the form of saline and glucose were supplied. Of 20 asthmatic patients who received an average of 2½ treatments a year, 12 had clinical remissions followed by attacks of less severity, frequency, and duration. Three other patients were clinically improved in that the attack ended more abruptly, and the subsequent attacks were less severe. Nine of 11 patients with hay-fever, who received 1 to 9 treatments, improved, one was free from symptoms for one season after treatment, and two for two seasons.

Hyde, R. W. (1940) *New Engl. J. Med.*, **222**, 839

Hay-Fever

Treatment

Adrenaline in oil.—The use of suspensions of powdered adrenaline in peanut oil having given such encouraging results in bronchial asthma, E. L. Keeney (1939) was led to investigate their effectiveness in the symptomatic control of seasonal and perennial hay-fever. The feature of such suspensions is that they are slowly absorbed and so the physiological activity of the active principle is prolonged. Natural and synthetic preparations of adrenaline were found to be equally effective. Of 35 patients to whom the treatment was given, 31 had been, and were, receiving specific desensitizing therapy. All had typical persistent symptoms of hay-fever. One or more subcutaneous injections of a 1 in 500 suspension, in doses ranging from 0.2 to 0.5 c.cm., were given to each patient at varying intervals. In most cases 0.3 c.cm. could be given without producing the unpleasant by-effects of the drug. Of the total number of patients, 30 obtained definite prolonged symptomatic relief, lasting from 12 to 36 hours after each injection, and 5 obtained no relief. The author recommends that, though this method should not replace specific desensitization therapy, it is valuable in the interval before such specific treatment is begun, in patients in whom symptoms persist in spite of specific therapy, and as a preventive measure in hay-fever patients who are on the verge of developing asthmatic symptoms.

Histaminase.—E. L. Keeney (1940) employed histaminase orally in 15 patients with typical ragweed hay-fever. The dosage ranged from 45 to 75 units daily. Pollen counts were made daily, and a daily symptom record was kept for each patient. Titrated intradermal tests with histamine acid phosphate were made before and after histaminase therapy. It was found that the drug failed to give relief to any of the patients, nor did it alter the histamine reaction in any case.

Potassium salts.—Since Bloom (1938) recommended the use of potassium salts for allergic conditions, various other authors, investigating the use of these salts, have been unable to reproduce Bloom's successful results. H. Miller and G. Piness employed potassium salts in 40 cases of hay-fever. Solutions containing 5 grains of

potassium chloride to the teaspoonful were given in doses of 3 to 4 teaspoonfuls a day to a group of patients. Later, the dosage was increased to 10 grains several times a day. Control solutions of sodium chloride and of potassium bicarbonate were also employed. In 38 cases no relief was obtained, and in the remaining 2 cases as much relief was obtained from the use of placebos as from potassium chloride solutions.

S. S. Rubin *et al.* also employed potassium salts in a series of 153 patients with hay-fever and seasonal asthma. Potassium chloride was given in doses of 10 to 15 grains, or potassium gluconate in doses of 15 to 30 grains, 3 or 4 times daily. The dose for children was from 5 to 10 grains of potassium chloride 3 or 4 times daily. The authors found potassium salts to be of no practical therapeutic value in these conditions.

W. C. Spain *et al.* report on the use of potassium chloride in 43 cases of allergy, including 31 of ragweed hay-fever and 12 of non-seasonal allergic coryza. Of the pollen cases 15 were treated with potassium chloride alone and 16 with potassium chloride and the usual specific injection therapy. The 12 cases of allergic coryza were given potassium chloride as an adjunct to the usual immunological procedures. As controls for the ragweed cases were 50 patients who received the standard pollen injection therapy without potassium therapy. The dosage of potassium chloride was 15 to 50 grains daily. The results of potassium therapy were disappointing. Of the 15 patients with hay-fever who received potassium chloride alone, 12 obtained no relief whatever from their symptoms. Of the 12 patients with allergic coryza, only 3 reported any definite relief of symptoms with the addition of potassium chloride to their routine treatment.

Bloom, B. (1938) *J. Amer. med. Ass.*, **111**, 2281.

Keeney, F. I. (1939) *J. Allergy*, **10**, 590.

— (1940) *J. Amer. med. Ass.*, **114**, 2448.

Miller, H., and Piness, G. (1940) *J. Amer. med. Ass.*, **114**, 1627.

Rubin, S. S., Aaronson, A. L., Kaplan, M. A., and Feinberg, S. M. (1940) *J. Amer. med. Ass.*, **114**, 2359.

Spain, W. C., Westcott, F. H., and Gaillard, G. I. (1940) *J. Allergy*, **11**, 388.

Vasomotor Rhinitis

Treatment

Histaminase — L. E. Prickman *et al.* employed an intestinal extract (histaminase) in 29 cases of vasomotor rhinitis. In 19 of the cases there was sufficient evidence from the results of cutaneous tests and in the clinical histories to suggest that the nasal symptoms were aggravated by the ingestion of specific foods. The others had vasomotor rhinitis which had been resistant to other forms of treatment. Nasal obstruction was constant in 19 cases, and intermittent in 10 cases. Eight patients were males, and 21 females; the ages ranged from 10 to 59 years. Of the patients, 12 (41·3 per cent) were relieved of the nasal obstruction, watery discharge and sneezing. Of those who obtained relief, a definite improvement in the appearance of the nasal membranes could be seen. Four patients (13·7 per cent) obtained a lesser degree of relief. The other 13 patients (44·8 per cent) did not obtain appreciable relief of the nasal symptoms. The dosage of histaminase employed was one or two tablets (5 to 10 histamine-detoxifying units) by mouth, 10 minutes before each meal.

Potassium salts — H. A. Rusk *et al.* made blood-potassium investigations of 55 patients with vasomotor rhinitis. They discovered that there was no significant change in the serum potassium of any of these patients, a fact which was in direct contrast to the authors' findings in urticaria and asthma. These patients were all advised to reduce materially the amount of sodium in their dietary, and were given either potassium chloride or potassium gluconate by mouth. The dosage of potassium chloride ranged from 30 to 90 grains per day, the drug being given in enteric-coated tablets after meals, and the dosage of potassium gluconate varied from 30 to 120 grains daily, given in plain tablets after meals. All the patients continued these drugs for at least 2 weeks after the onset of symptoms. In some patients 2·5 and 5 per cent solutions of potassium chloride were employed intra-

nasally without appreciable effect. Of 30 of these patients who were suffering from ragweed hay-fever, only 9 per cent obtained marked relief from the use of potassium salts, whereas in other types of nasal allergy, potassium salts were very effective.

Prickman, L. E., Illie, H. I., Roth, G. M., and Fleming, R. G. (1940) *Ann. intern. Med.*, **13**, 2235.

Rusk, H. A., Dean, L. W., Jr., and Rindskopf, W. (1940) *Ann. Otol., etc., St. Louis*, **49**, 76.

Skin Manifestations

Treatment

Histaminase.—A. R. Altose employed histaminase in 18 cases, 7 of urticaria, 4 of angioneurotic oedema, 3 of urticaria and angioneurotic oedema combined, and 4 of allergic dermatitis. The drug was given orally or parenterally. The average duration of treatment was 11.4 days. The minimal total dosage was 20 units, and the maximal 600 units, with an average of 245 units. The daily dosage ranged from 45 to 75 units. Of the 18 cases, 8 were greatly improved, 6 were moderately improved, and 4 were unimproved.

Altose, A. R. (1940) *Northw. Med., Seattle*, **39**, 212.

Cold Allergy

Treatment

Histaminase and desensitization.—I. W. Baker successfully employed a combination of systemic desensitization to cold and the oral use of histaminase in two cases of cold allergy. Histaminase is a protein-like material derived from the intestinal mucosa, and is said to be destructive to histamine and histamine-like substances. It is prepared in enteric-coated tablets, each representing 5 histamine-detoxifying units, or in ampoules, each dose being equivalent to two histamine-detoxifying units. One unit represents the quantity of histaminase which is capable of detoxifying 1 mg. of histamine hydrochloride during 24 hours at 37° C. The course of treatment lasted for 5 weeks. During the first week the hands were immersed in ice water, twice daily for one minute. During the second week the time of immersion was increased to 2 minutes, twice daily, and so on until the fifth week, when the immersion was for 5 minutes, twice daily. Simultaneously two tablets of histaminase, each containing 5 units, were given orally for the first two days, and thereafter 3 tablets daily. The total number of tablets employed during the 5 weeks was 103, or 515 units. After treatment the patients could handle ice and disregard cold without untoward results.

Baker, T. W. (1940) *J. Amer. med. Ass.*, **114**, 1059.

Gastro-Intestinal Allergy

In Children

Treatment by allergens.—J. H. Fries and J. Zizmor describe the clinical manifestations of gastro-intestinal allergy in children. Allergens were given orally to 30 children and rectally to 16. Symptoms following oral ingestion were nausea in 43 per cent of cases, vomiting in 23 per cent, abdominal pain, generally near the umbilicus, in 20 per cent, and burning in the mouth and an itching in the throat with circumoral erythema and swelling of the lips in 2 cases. Clinical manifestations were not observed in 8 of the cases. In the cases in which the allergen was given rectally there was abdominal pain shortly after administration in 75 per cent; in some instances this pain was severe, cramp-like, and localized in the middle or upper abdominal regions. In 25 per cent of cases tenesmus immediately followed administration. There were no clinical manifestations in 3 of the cases in this group. Constitutional reactions occurred in 2 patients after oral ingestion, and in one patient after rectal administration. In the oral cases these reactions were of moderate intensity, but in the rectal case they were severe and required adrenaline for their control. These general symptoms included urticaria, pruritus, dyspnoea, wheezing, cyanosis, faintness, rapid pulse, congestion of the conjunctivae, and lacrimation.

Fries, J. H., and Zizmor, J. (1940) *J. Pediat.*, **16**, 69.

Genito-Urinary Manifestations*Treatment*

Histaminase. - H. M. Johnson stated that certain urological symptoms exist which appear to be correlated with other conditions having an allergic basis. He described several such cases which included pruritic skin rashes, herpes zoster, food allergy, rhinitis, nervousness, indigestion, eczema, migraine, impotence, constipation, always associated with urinary symptoms such as burning, frequency, and backache, on the basis that histaminase, which is derived from the intestinal mucosa, is the natural enzyme neutralizing histamine, which when improperly detoxified is largely responsible for allergic manifestations. The author employed histaminase in 37 cases exhibiting urological symptoms associated with allergy. In all cases symptoms were definitely improved or entirely relieved by such treatment. The dosage employed varied, the initial dose was generally 5 units, one to three times a day, but some obstinate cases required 10 units, three times a day. At the same time as the histaminase was being employed by mouth, active desensitization was also effected by intradermal injections of 0.05 c.c. of a 1 in 5,000 solution of histamine acid phosphate, every day for 1 to 8 weeks, depending on the severity of the condition being treated.

Johnson, H. M. (1940) *J. Urol.*, **43**, 891.

Allergic Conditions Generally*Treatment*

Reactions from adrenaline in oil. - A. L. Maietta stated that, although adrenaline in oil gives good results in the symptomatic relief of allergic states, certain transitory systemic and local reactions may occur following its use. Of 14 patients treated by the subcutaneous injection of 0.4 c.c. of adrenaline hydrochloride solution 1 in 1,000, followed in 10 minutes by the intramuscular injection of 1 c.c. of sterile peanut oil containing 2.0 mg. of adrenaline, reactions occurred. In one case the reactions consisted of cold hands and feet, chilly sensations, clammy perspiration, facial pallor, frontal headache, and cardiac palpitation. In the other case local manifestations were a preliminary blanching followed by redness, intense itching, marked oedema, and induration at the site of the injection.

Histaminase. - H. Miller and G. Piness report on the results of histaminase administration in 42 patients with allergic manifestations, namely urticaria (29), chronic allergic dermatitis (5), allergic bronchial asthma (5), and chronic nasal allergy (3). In no case was there definite evidence that this enzyme was responsible for the relief or prevention of any of the signs or symptoms of which the patients complained. The average dosage of histaminase was from 60 to 75 units in 24 hours, with a maximum of 102 units, and the longest period of consecutive treatment was 108 days.

Potassium chloride. - G. I. Harsh and P. B. Donovan employed potassium chloride in 40 cases of various forms of allergy, but chiefly hay-fever. Negative or questionable results were obtained in all but one case. The dosage varied from 0.33 to 4 g. potassium chloride daily. In some cases sodium chloride in the diet was restricted. In 18 of the cases the serum sodium was estimated before and after the medication, and in 15 of these patients the serum potassium was also estimated. No significant alteration in the concentration of either ion was found.

Propadrine hydrochloride. - J. A. Murphy reported 16 cases of allergic illness which were treated with propadrine hydrochloride (α -hydroxy- β -aminopropylbenzene hydrochloride). The drug is a bronchodilator and local vasoconstrictor. The cases treated included asthma, hay-fever, and urticaria. The usual dose for adults was $\frac{1}{2}$ grain; children do better on $\frac{1}{4}$ grain. The treatment was very successful, the drug acting very like ephedrine except that it produced none of the unpleasant side-effects of ephedrine. Like ephedrine, it had no effect upon very severe attacks of asthma or hay-fever.

Harsh, G. I., and Donovan, P. B. (1940) *J. Amer. med. Ass.*, **114**, 1859.

Maietta, A. L. (1940) *New Engl. J. Med.*, **222**, 715.

Miller, H., and Piness, G. (1940) *J. Amer. med. Ass.*, **114**, 1742.

Murphy, J. A. (1939) *Penn. med. J.*, **43**, 65.

ALOPECIA

See also B I: M P, Vol. I, p. 337

Alopecia totalis*Aetiology*

Relation to dysfunction of pituitary—F. Kylin and E. Dicker examined 29 cases of total alopecia. In many cases alopecia is hereditary; of the 29 cases, 9 gave a definite history of heredity. The general health was never affected; the blood sugar was within normal limits and libido was normal. The incidence is the same in both sexes and any age may be affected, though there seems to be a certain predilection at the age of about 25 years. None of the patients was hypertensive, but some were hypotensive. Of 4 cases examined radiologically, 3 showed a sella turcica slightly smaller than normal. Among 16 females, 6 were starting their first menstruation, and 3 of the 16 had not menstruated until relatively late, 17 to 19 years. In 15 there was depigmentation of the skin, 14 had dental caries, and in about half anxiety, headache, and asthenic symptoms were present when the first sign of alopecia appeared. Half of them were constipated. The disease is characterized by a general loss of hair of the body with changes in the skin and nails, accompanied by anxiety, a feeling of cold, and asthenia. It resembles the condition caused by functional changes of the pituitary.

The endocrine glands influencing the hair and its growth are the gonads, the adrenals, the thyroid, parathyroids, and the pituitary. None of these patients showed signs of eunuchoidism or sterility. The only connexion with the gonadal hormones is the relation between the first menstruation and the first appearance of the alopecia. There is a dysfunction of the adrenals, as shown by symptoms of hypertrichosis and some adrenal tumours. Brittleness of the nails has been observed and might be the result of a thyroid disturbance. Most of the patients show symptoms of pituitary disorder, such as anxiety states, insomnia, hypoglycaemia, decrease of basal metabolism, diminution of menstruation, skin changes, and loss of libido. Changes in the pituitary function are regarded as of the utmost importance and dominate the picture in total alopecia.

For treatment, transplantations of calf's total pituitary is suggested; this gives better results than injections of pituitary substance or ingestion of pituitary extracts.

Treatment

Endocrine therapy—The results obtained by workers in the treatment of alopecia areata and totalis with endocrines have varied. J. L. Thorner reports the case of a woman, aged 32 years, whose hair entirely disappeared from the head, face, and body when she was 3 months pregnant; the process began two months before pregnancy. The patient's thyroid had been operated on for pressure symptoms 6 years previously, and since then she had been taking thyroid tablets daily. She began to go bald during her first pregnancy 2 years previously, but not until the second pregnancy did the loss of hair become extensive. Four months after the birth of the second baby she was treated with pituitary extract for 26 days. A fine colourless lanugo appeared on the scalp. After 2 months' treatment the injections were stopped because the breasts became painful. The patient was not seen again for about 16 months. She then had 18 patches of dark hair on the scalp, and her eyelashes and facial lanugo had partly returned. She was placed on progynon-B by injection and progynon-DH by mouth. The hair of her scalp then became more abundant, as did the pubic and axillary hair. There was a family history of endocrine imbalance, two members having undergone thyroidectomies for pressure symptoms. One other member of the family suffered from alopecia during pregnancy and a fourth member had symptoms suggesting acromegaly.

Kylin, F., and Dicker, E. (1939) *Acta med. scand.*, **100**, 485.

Thorner, J. F. (1940) *Endocrinology*, **26**, 433.

Alopecia of Peroneal Region*Sign of Neuro-Arthritic Diathesis*

L. Tommasi described the presence of a symmetrical alopecia on the antero-lateral

and postero-lateral aspects of the legs, and especially of their lower two-thirds. The alopecia consists of round or oval patches with well-defined margins, stopping sometimes in the median longitudinal line of the calf. The skin is usually smooth and thin. This condition, which is most common between the ages of 40 and 60, is held by the author to be a diagnostic sign in neuro-arthritis and was present in 15.5 per cent of a series of cases of skin diseases in which an altered purine metabolism was suspected. It was sometimes present in subjects who were otherwise bald, but it was more frequently a localized manifestation.

Tommasi, L. (1940) *Brit J. Derm.*, **52**, 1

ALZHEIMER'S DISEASE

See also B.F.M.P., Vol. I, p. 354, and Surveys and Abstracts 1939, p. 202

Clinical Picture and Morbid Anatomy

W. H. McMenemy *et al.* published a case of presenile dementia (Alzheimer's disease) with a positive family history of the condition. The patient was an intelligent gifted man of 51 years who had been failing mentally for 5 or 6 years. His power of concentration, memory, and enthusiasms progressively decreased. A year after the onset of the mental symptoms he had noticed some stiffness in his limbs. On examination he was found to be grossly demented and spastic. There were no typical signs of Parkinsonism. His condition gradually became worse and finally he became bedridden and died. Autopsy showed typical changes of Alzheimer's disease. There was extensive degeneration of the nerve cells and many senile plaques in the brain. Investigation revealed that 3 out of 4 siblings in the previous generation suffered from presenile dementia. Their parents were first cousins. One of them was the father of the patient reported.

McMenemy, W. H., Worster-Drought, C., Hind, I., and Williams, H. C. (1939) *J. Neurol. Psychiat.*, **11**, 293

AMENORRHOEA

See also B.F.M.P., Vol. I, p. 359, and Surveys and Abstracts 1939, p. 202

Aetiology

Secondary Amenorrhoea

Due to general or constitutional causes: tuberculosis.—I. Pedrini discussed the association between amenorrhoea and pulmonary tuberculosis, which, in his opinion, is of great diagnostic importance. In over 60 per cent of his cases of pulmonary disease in young women amenorrhoea was present, the longer this amenorrhoea lasted and the more marked it was, the worse the prognosis. He emphasized that general treatment of the pulmonary condition should be the only treatment and that the amenorrhoea, always secondary, should be left alone. The return of menstruation was often the precursor of definite improvement in the clinical condition.

Pedrini, I. (1939) *Giorn. medica dell' Alto Adige*, **11**, 332

Delayed Menstruation

Treatment

Prostigmin.—S. Soskin *et al.*, on the basis that hyperaemia plays an important role in the phenomenon of oestrus, suggested that delayed menstruation might be due to lack of vascular response rather than to endocrine dysfunction. Accordingly they tried the effect of prostigmin in 25 cases of delayed menstruation in which pregnancy was excluded by the history and physical examination, supplemented when necessary by the Friedman test. It was found that prostigmin invariably precipitated the menstrual flow, in one case as soon as half an hour after one injection; the longest interval between the last injection and the beginning of the

flow was 78 hours. The dosage employed varied from 1 to 3 intramuscular injections of 1 or 2 c.cm. of a 1 in 2,000 solution of prostigmin methylsulphate. Preliminary work on animals, and then on 23 human subjects conclusively showed that the drug did not initiate menstrual flow when the delay was due to early pregnancy. Neither did the drug have any effect in early or prolonged amenorrhoea due to endocrine dysfunction or to local organic changes. The authors suggested that this work might be the basis of a new test for pregnancy.

Soskin, S., Wachtel, H., and Hechter, O. (1940) *J. Amer. med. Ass.*, **114**, 2090.

AMOEBIASIS

See also B F M P, Vol. I, p. 366, and Cumulative Supplement, Key No. 56

Protozoology and Pathology

Associated with Balantidium coli Infection

H. G. Hummel reports the case of a man, aged 49, with an amoebic granuloma of the rectum associated with *Balantidium coli* infection. Sigmoidoscopic examination showed a soft, greyish-pink, granulomatous growth the size of a large walnut, on the wall of the rectum, and discrete punched-out ulcers scattered over the walls of the rectal ampulla and sigmoid, these ulcers were irregular in outline, averaging about $\frac{1}{2}$ to 1 cm. in diameter, and bleeding readily when scraped. Scrapings from the ulcers revealed the presence of *Balantidium coli*. Scrapings from the tumour showed the presence of *Entamoeba histolytica*.

Hummel, H. G. (1940) *Amer. J. digest. Dis.*, **7**, 178.

Clinical Picture

Liver Abscess

Symptomatic pleurisy—C. Anagnostopoulos stated that symptomatic right pleurisy is a serious complication of amoebic hepatic abscess. The diagnosis often proves difficult. The presence of amoebic elements in the stools is helpful. Search for the painful spot by digital pressure on the lowest intercostal spaces, and exploratory puncture of the liver at this point may clear up the doubt.

Anagnostopoulos, C. (1940) *Pr. méd.*, **48**, 7.

Diagnosis

Amoebic Granuloma Simulating Carcinoma of Rectum

C. J. Donald and P. W. Brown report two cases in men, aged 53 and 54, of granulomatous masses in the rectum, which imitated primary carcinoma, but were associated with the presence of *Entamoeba histolytica*, and disappeared after treatment by emetine hydrochloride and trepanol, this combination being the most effective anti-amoebic treatment. As *Entamoeba histolytica* may occur in the rectum with a primary carcinoma, the use of various diagnostic procedures is advisable.

Donald, C. J., Jni., and Brown, P. W. (1940) *Proc. Mayo Clin.*, **15**, 321.

Amoebic Dysentery

Treatment

J. G. Mateer *et al.* pointed out that the most effective amoebicidal drug now known fails to effect a permanent cure in 10 per cent of cases, when used alone and in a single course of treatment. There are disadvantages to any method which requires repeated courses of treatment. A simple method of combined drug treatment which has reduced the percentage of failures from 10 to 3 was described by the authors. The method consists of administering by mouth a single course of carbarsone, consisting of 0.25 g. before breakfast and supper each day for 10 days, and simultaneously giving 250 c.cm. of a 2.5 per cent chiniofon solution as a high retention enema every other day during this 10-day period. The clinical material utilized consisted of an unselected group of 104 cases of uncomplicated amoebiasis. The

cases were followed up for periods varying from 6 months to 3½ years. It was found that, employing the above method, there was persistent absence of amocbae from the stools in 97 per cent, or 101 out of the 104 cases

Mateer, J. G., Baltz, J. I., Marion, D. F., and Hollands, R. A. (1940)
Amer. J. digest Dis., **7**, 154

AMPUTATION

See also B E M.P., Vol. I, p. 378, Surveys and Abstracts 1939, p. 202; and p. 11 of this volume

Complications of Amputation

Post-Amputation Pain

Treatment with vitamin B₁—A Shlosberg employed vitamin B in the treatment of post-amputation pain. Of 67 cases there was 100 per cent relief in 11, from 50 to 90 per cent relief in 39, and from 30 to 40 per cent relief in 10; and from 10 to 20 per cent relief in 7. Apart from subjective relief, there was a definite reduction of arterial hypertension. In 45 cases relief was obtained with 5 or fewer injections. The dosage was 1 cm. subcutaneously every other day.

Shlosberg, A. (1939) *Pr. méd.*, **47**, 1589.

ANAEMIA

See also B I M.P., Vol. I, p. 408; Cumulative Supplement, Key No. 59; Surveys and Abstracts 1939, pp. 53 and 203, and p. 32 of this volume

Pernicious Anaemia

Aetiology

The argentaffine cells and pernicious anaemia—W. Jacobson brings forward evidence that the argentaffine cells play a part in the normal formation of red blood-corpuscles. In 12 cases of pernicious anaemia there was a complete absence in 6, and in the other 6 an almost complete absence of the argentaffine cells throughout the gastro-intestinal canal; in 2 cases of sprue with macrocytic anaemia there was an almost complete absence of the argentaffine cells, in macrocytic anaemias not responding to liver treatment (3 cases), and in secondary anaemia, the argentaffine cells were either not affected or affected only in a slight degree. The argentaffine cells contain yellow granules, which contain a pterine and a carbohydrate. Pterines, made up of 3 purine groups and found on the wings of butterflies, may influence the process of haematopoiesis. The argentaffine cells occur in the cardia and pylorus, being practically absent from the body of the stomach, are very numerous in the duodenum, and also occur in the small intestine, colon, and vermiform appendix; they are specifically differentiated cells of the intestinal epithelium. They make up the carcinoid tumours of the appendix and small intestine. Isolation of the granules in these cells is one of the most important points in solving the problem of the relation of the argentaffine cells to the formation of red blood-cells.

Clinical Picture

Jaundice associated with pernicious anaemia.—M. Chiray *et al.* described a case of haemolytic icterus and discussed whether it should be classified in the group of haemolytic diseases or in the group of Biermer's anaemia. The patient, a woman of 54, was admitted to hospital with severe asthenia, some icterus, 1,552,000 red blood-corpuscles, and 45 per cent haemoglobin (colour index 1.45). The authors diagnosed pernicious anaemia with icterus, and gave liver extracts by mouth, together with injections of liver extract. A blood transfusion was made, but the condition of the patient deteriorated. The number of erythrocytes decreased, the jaundice became accentuated, and the spleen was somewhat enlarged. It was decided to remove the spleen. There was a rapid improvement after the operation, and the patient left hospital 40 days later. She had, however, to return to hospital twice, on each occasion after an interval of 6 months, but treatment with liver extract improved her condition. During the remissions she had anaemic symptoms

but no icterus, and there was no diminution of the resistance of the erythrocytes. The authors concluded that the patient had pernicious anaemia, proved by the typical blood picture and by the result of gastroscopy which demonstrated atrophic spots. The ineffectiveness of liver therapy was due to insufficient dosage. The further development of the case, especially the 2 remissions, are also in favour of the diagnosis of pernicious anaemia. Icterus with pernicious anaemia is not rare. The authors described the morbid changes in the spleen and found that they corresponded with those described as typical of pernicious anaemia by Lubarsch and Lippinger, namely lesions of the arterioles, active congestion of lymphatic nodules, and ferrous pigmentation.

Angina.—S. Vatcher reported a case of pernicious anaemia complicated by angina pectoris. The electrocardiograph showed negative T waves and left ventricular preponderance until the patient improved under liver therapy, when it became normal. The patient also had an abdominal aneurysm, the diagnosis being confirmed by X-ray examination owing to the presence of calcification. Electrocardiographic changes are not usually present in angina associated with pernicious anaemia. Owing to the presence of the calcified aneurysm in spite of a negative Wassermann reaction, Vatcher concluded that arteriosclerotic changes were also present in this case leading to some coronary stenosis. At one stage the electrocardiographs were suggestive of this condition.

Associated tuberculosis of the stomach.—A. Schweers described a case of pernicious anaemia in which, five years after treatment for the condition, tuberculosis of the stomach developed. This coexistence is extremely rare, and the author explained its occurrence only on the assumption that pernicious anaemia set up a locus minoris resistentiae in the gastric mucosa as a result of the temporary lack of the Castle factor. Such a case would not have occurred formerly, because the patients died long before such a change could have taken place, and thus modern liver therapy was responsible for allowing a secondary disease of importance to develop in a patient suffering from pernicious anaemia.

Prognosis

C. C. Sturgis has analysed 147 cases that proved fatal out of 542 patients treated by Minot and Murphy's liver treatment at the Simpson Memorial Hospital at Ann Arbor. Among the 147 patients 90 were males and 57 females, thus differing from the general impression that the sex incidence is equal. The earliest symptoms of the disease occurred at or over 50 years of age in approximately 70 per cent of the fatal cases, and achlorhydria was present in all; necropsies were obtained in 23 cases only. On admission 88 per cent of the patients had symptoms referable to the nervous system; in 25 per cent these consisted only of paraesthesia of the hands and feet; 24 per cent had paraesthesia and also symptoms and signs indicating involvement of the posterior columns of the spinal cord; 39 per cent had paraesthesia and involvement of the posterior and lateral columns, and 16 per cent had combined degeneration with definite disturbance of the urinary bladder. Approximately a third (47) of the patients died of some unknown cause, another third (51) succumbed to pernicious anaemia, 44 to involvement of the nervous system, and only 7 to anaemia. In the remaining third (49) death was due to some unrelated disease, cardiac (11), cancer (11), hemiplegia (7), pneumonia (5); in one case only was tuberculosis responsible. The worst prognosis was in patients who had lost vesical control as the result of spinal cord changes. It was also concluded that patients ran an equal chance of dying from pernicious anaemia or from some unrelated condition, and that the prognosis for duration of life is directly related to the extent of involvement of the nervous system. There are, however, some remarkable instances of long periods of survival in patients with advanced diseases of the spinal cord, and with improved methods of treatment with parenteral administration better results should be expected.

Diagnosis and Prognosis

Excretion of volatile phenols.—M. Volterra examined the volatile phenols in the urine of patients with pernicious anaemia and found their amount to be a valuable diagnostic and prognostic sign. He observed that before treatment the amount of volatile phenols in the urine was very low (6 to 23 mg. in 24 hours), the amount

corresponds with the severity of the anaemia as judged by the number of red corpuscles. The volatile phenols are greatly increased in amount during treatment with liver extracts and can quickly reach 100 mg. If the hepatic treatment does not influence the phenol excretion, it also does not influence the blood picture. Liver therapy in non-pernicious anaemia does not greatly influence the blood picture or the phenol excretion.

Treatment

Capacity to store injected liver extract—M. B. Strauss and F. J. Pohle tried to determine the capacity of patients with pernicious anaemia to store injected liver extract in excess of the immediate requirements, and whether rapid depletion or inability to utilize such stored material may render large injections at long intervals unsatisfactory. It was found that patients with pernicious anaemia who require relatively little liver extract to maintain a normal blood-level may relapse in as short a time as 2 months after liver therapy is omitted. The majority of patients could not be successfully treated with massive doses of liver extract given at intervals of several months. The optimal interval between injections for most patients with pernicious anaemia was from 1 to 4 weeks.

Nervous symptoms vitamin B₁₂ therapy. Funicular myelitis has often arisen in cases of pernicious anaemia, the nervous symptoms of which often persist after the blood picture has been restored by liver therapy. I. Sciclounoff and M. Naville observed 13 cases of pernicious anaemia, in the majority of which, while blood had become normal after liver therapy, the nervous symptoms persisted. With vitamin B₁₂ therapy improvement or complete cure was observed in 8 cases. The dosage was 4 to 10 mg. of vitamin B₁₂ daily for 3 weeks, many cases improved during the first week of treatment.

Chiray, M., Albot, G., and Scemama, J. (1939) *Bull. Soc. méd. Hop. Paris*, **55**, 1069.

Jacobson, W. (1939) *J. Path. Bact.*, **49**, 1.

Lubarsch, O. (1927) *Handbuch der speziellen pathologischen Anatomie und Histologie* (Henke, F., and Lubarsch, O.), Berlin, Bd. **1-2**, p. 616.

Schweers, A. (1939) *Zbl. inn. Med.*, **60**, 737.

Sciclounoff, I., and Naville, M. (1940) *Schweiz. med. Wschr.*, **70**, 166.

Strauss, M. B., and Pohle, F. J. (1940) *J. Amer. med. Ass.*, **114**, 1318.

Sturgis, C. C. (1939) *Trans. Ass. Amer. Phys.*, **54**, 46.

Vatcher, S. (1939) *Lancet*, **2**, 192.

Volterra, M. (1939) *Schweiz. med. Wschr.*, **69**, 627.

Achrestic Anaemia

M. C. G. Israels and J. F. Wilkinson in their new observations on the aetiology and prognosis of this form of hyperchromic megalocytic anaemia now follow up their full description in 1936. The blood picture and bone-marrow changes are exactly the same as in Addisonian pernicious anaemia, but it differs in the presence of hydrochloric acid in the gastric juice, the progressive and eventually complete failure to respond to the treatment successful in pernicious anaemia, the progressive fatal course, and the presence in the liver of adequate amounts of the anti-anaemic principle, the disease is regarded as due to failure to utilize the principle or to mobilize it from the stores in the tissues. It is a rare condition, occurring in 1 per cent of cases of pernicious anaemia. In 1938 the authors found among 1,100 patients 1 example of achrestic anaemia with achlorhydria. To meet criticism of this separation of a very grave anaemia from the Addisonian form 6 new cases are reported in detail, special stress being laid on sternal puncture which showed in all the 6, still living, patients typical megaloblasts and in some early normoblasts. The difficulty of diagnosis from aplastic anaemia should be met by the absence from the bone-marrow in aplastic anaemia of real megaloblasts. Of the 6 new cases 3 were in young women and in these the condition resembled in some respects the so-called 'pernicious anaemia of pregnancy', though none of these 3 patients was pregnant. There is reason to hope that the prognosis is better in these young women than in the disease achrestic anaemia as originally described.

Treatment.—Patients with achrestic anaemia should first be given the specific anti-pernicious-anaemia treatment in larger doses and for a longer time than in ordinary pernicious anaemia, and the preparation should be one of the less highly purified extracts for intramuscular injection, because there is some evidence that the more highly purified liver extracts may not contain all the active material. Blood transfusion seems necessary for most of the patients sooner or later, but in young women it may be required only to tide over a specially difficult period.

Israels, M. C. G., and Wilkinson, J. F. (1936) *Quart J Med*, N S **5**, 69.

— (1938) *Lancet*, **2**, 362.

— (1940) *Quart J Med*, N S **9**, 163.

Megalocytic Anaemia of Pregnancy

Aetiology

Lowered gastric secretion—J. S. Labate analysed the gastric juice in 56 pregnant women because lowered gastric secretion has been stated to be of aetiological significance in the megalocytic anaemia of pregnancy. All but 2 of the women were in the last 3 months of pregnancy, and 35 of them were in the last month. Nine of the series showed hypochlorhydria and 5 complete post-histamine achlorhydria. The red blood-cell count and haemoglobin decreased as the gastric acidity diminished but, according to Labate, this does not prove that achlorhydria is an important aetiological factor in the anaemias of pregnancy.

Labate, J. S. (1939) *Amer J Obstet Gynaec*, **38**, 650.

Hyperchromic Anaemia of Pregnancy

Treatment

Cholesterol.—H. N. Chatterjee stated that one of the commonest forms of anaemia in India is seen in conjunction with pregnancy. The anaemia is commoner in young women, in the earlier pregnancies, and most of the cases have some secondary infection. The blood picture varies. It may be macrocytic, microcytic, hyperchromic, or hypochromic. The same case may go through the different varieties, depending on its severity and whether it is progressing or recovering. The van den Bergh reaction is negative and most of the cases have free acid in the stomach. The serum globulin is very high, the increase being in the euglobulin fraction. The blood cholesterol is low, and this led Chatterjee to treat 14 cases with 2 c.cm. of a 5 per cent solution of cholesterol in olive oil intramuscularly every other day. These patients all improved, while the condition of 2 controls, treated with iron and campolon (liver extract), deteriorated.

Chatterjee, H. N. (1940) *Lancet*, **1**, 14.

Haemolytic Anaemias

Radiological Changes in the Bones of Children with Anaemia

C. G. Teall, radiologist to the Birmingham Children's Hospital, and a colleague of L. G. Parsons, describes the radiological appearances of the bones in anaemic children. In deficiency or anhaematopoietic anaemias the bone marrow shows hypoplasia. In haemolytic anaemia, more accurately called by Parsons erythroclastic, such as icterus gravis neonatorum and congenital haemolytic anaemia, the bones do not show any radiological changes. The subacute forms are accompanied by osteoporosis and thinning of the cortical bone, the osteoporosis of the long bones being most prominent in the metaphyses. In subchronic forms, which include the heterogenous cases described under the title of von Jaksch's anaemia, the osteoporosis is more advanced and the long bones show a more open-work trabeculation near their ends; the change in the bones progressively increases with the chronicity of the anaemia.

Teall, C. G. (1939) *Brit J. Radiol*, **12**, 601.

Atypical Haemolytic Anaemias

F. G. Lescher and G. R. Osborn reported 2 cases of atypical haemolytic anaemia. The first case was that of a woman of 55 years showing all the signs and symptoms

of severe anaemia. In addition she was markedly jaundiced, although her stools were normal in colour, and her blood showed the abnormally high reticulocyte count of 90 per cent. She was treated with liver extract, iron, and blood transfusions, and eventually her spleen and an accessory spleen were removed. After a stormy convalescence the patient completely recovered. The second case showed the Marchiafava-Micheli syndrome in a man aged 39 years. The patient had a macrocytic anaemia and haemoglobinuria. The Kahn reaction for syphilis was positive on 3 occasions. The haemolysis in these conditions was found to occur because of abnormality in the red cells. Haemolysin, usually present in the blood plasma, was absent from it in the second case.

Lescher, I. G., and Osborn, G. R. (1939) *Quart. J. Med.*, **8**, 335.

Erythroblastaemia

I. Parkes Weber reviews the aetiology of erythroblastaemia, or the presence of nucleated red cells in the circulation, and especially the value of this blood change in the diagnosis of neoplastic infiltration of bone marrow. It is difficult to decide whether the latter erythroblastaemia is part of an attempt to compensate for destruction of the bone marrow by the malignant cells, or whether it should be regarded, at least in part, as due to some other form of excitation of the erythroblastic elements in the bone marrow by direct contact with the infiltrating neoplastic cells, but probably these 2 causal factors work together in varying proportion in different cases. This neoplastic infiltration is nearly always secondary to carcinoma and rarely to sarcoma, these patients are mainly the subjects of primary carcinoma of the prostate which may not be enlarged. Apparently millions of malignant cells are poured into the blood stream, and mainly held up in the bones and bone marrow, the innumerable metastases each consisting of a few cells only. This may explain some of the rheumatic pains and malaise. Obviously other tissues are infiltrated, but the cells may atrophy and not cause gross metastases. It is not clear why in some rather rare cases of secondary neoplastic infiltration of the skeleton, new bone is formed instead of absorption of bone. The osteoplastic change increases not only the weight but the thickness of the affected bones, and has been called 'secondary marble bones' (Weber, 1935) in contrast to the rare developmental condition of marble bone described by Albers-Schonberg. Recognition of erythroblastaemia is of value in cases in which radiograms show symmetrical uniform osteosclerosis of the pelvis, an example of which is given. It is pointed out that erythroblastaemia may occur in all leukaemias.

Weber, F. P. (1935) *Lancet*, **1**, 377.

-- (1940) *ibid.*, **1**, 1077.

Cooley's Erythroblastic Anaemia

A. Francaviglia described three cases of Cooley's erythroblastic anaemia. The patients, all children, were of the mongoloid-negro type, and their blood showed marked changes towards the embryonic state; in addition there were anisocytosis, poikilocytosis, reticulocytosis, and leucopenia. The facial and cranial bones were hypertrophied, and the rest of the skeleton showed osteoporosis. Administration of thyroid, liver extracts, and iron seemed to have a beneficial effect on the condition.

Francaviglia, A. (1939) *Arch. Sci. med.*, **68**, 395.

ANAESTHESIA

See also B. F. M. P., Vol. I, p. 472, Cumulative Supplement, Key No. 60, Surveys and Abstracts 1939, pp. 25, 163 and 207, and p. 108 of this volume.

Inhalation Anaesthesia

Respiratory Physiological Phenomena

F. B. Tuohy emphasizes the importance, in pre-operative anaesthesia, of giving such drugs as morphine and atropine in doses suitable for the individual case and at an interval before anaesthesia sufficient to secure their satisfactory action. During

anaesthesia stridor may prevent the proper diffusion of the anaesthetic through the lungs; this may be due to the tongue falling back and obstructing the airway, when a pharyngeal, intratracheal, or mouth airway tube should be inserted. Too rapid administration of the anaesthetic may irritate the vocal cords and produce stridor, and too concentrated an anaesthetic mixture should be diluted with oxygen. Traction on viscera may also produce stridor, which is best overcome by intratracheal intubation. Chemical agents by increasing the hydrogen-ion content of the cells in the medulla and afferent nerve impulses from the lungs (the Hering-Breuer reflex) physiologically influence respiration during anaesthesia. If anoxaemia is produced, oxygen should be given at once. Because the anaesthetic agent is eliminated more slowly than it is taken up from the lungs, hyperventilation with oxygen and then air should be performed at the end of anaesthesia. If circulatory and respiratory depression supervene during anaesthesia, the patient's lungs should be ventilated with oxygen, and intravenous fluids administered. In impending shock vasoconstrictor stimulants, such as adrenaline, should be avoided if the blood vessels are already constricted; they are best given when the systolic blood-pressure is not below 70 or 80 mm. Hg. It is better first to restore the circulating blood-volume by means of intravenous fluids.

Tuohy, E. B. (1939) *Arch. Surg., Chicago*, **39**, 1001

Endotracheal Anaesthesia

Advantages and Disadvantages

R. M. P. Milne and J. R. Mackenzie discussed the advantages and disadvantages of endotracheal anaesthesia. The method can be used with advantage to both patient and surgeon in long difficult operations. A minimum of anaesthetic can be given with the maximal amount of control and, should collapse or shock supervene, the best apparatus for the administration of artificial respiration is already in position. The disadvantage is that laryngitis, tracheitis, haemorrhage from the nose or pharynx, or granuloma of the vocal cords may follow the passage of the tube. To prevent unpleasant sequelae the tube should not reach the bifurcation of the trachea or it may enter a bronchus, causing collapse of the other lung. The bore of the tube should be such that it is not in constant contact with the vocal cords. The tube should be lubricated and the nose and pharynx sprayed with 10 or 20 per cent cocaine before it is passed. Blind intubation should never be attempted, except in those rare cases in which direct vision is impossible. In a teaching hospital it is advisable to use the simple, more portable forms of anaesthesia whenever possible, so that the student may become familiar with them.

Milne, R. M. P., and Mackenzie, J. R. (1939) *Brit. med. J.*, **2**, 1136

Anoxia

R. D. McClure *et al.* state that anoxia may generally be demonstrated during anaesthesia induced by present-day methods, thus narcotics, especially morphine and barbiturate derivatives, in moderate to large doses, tend to produce anoxia, especially of the histotoxic type. Destruction of individual cells, vital organs, and even life is most liable to result when a severe histotoxic anoxia is accentuated by one or more of other types, anoxic, stagnant, or anaemic anoxia. Full consideration of anoxia as a cause of surgical complications should reduce pre-operative narcotics to a minimum, promote the use of anaesthetics which allow adequate oxygen in the inspired air, and emphasize the necessity of maintaining the blood pressure and respiration at nearly normal levels.

McClure, R. D., Hartman, F. W., Schnedorf, J. G., and Schelling, V. (1939) *Ann. Surg.*, **110**, 835

Sedative Effect of Oxygen

C. Flandin *et al.*, in the course of research on oxygen therapy, found a surprising somnifacient and sedative action from oxygen administered by a mask. The suggested explanation is that oxygen saturation of the nervous centres counteracts the polypnoeic and dyspnoeic effect of carbon dioxide. A 67-year-old patient was

admitted to hospital with delirium tremens after pneumonia, and with hallucinations and poor general condition. Ammonium acetate, strychnine, and digitalis were administered, but without success. The patient was cyanotic and had a polypnoea of 36 per minute. He was put into an oxygen tent, and after a few minutes he became calm and nearly asleep. Tremor and cyanosis disappeared. After 3 hours, the polypnoea was reduced to 28 movements per minute; when again placed under the tent, he soon recovered completely.

Flandin, C., Breton, P., and Lemaire, R. (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 1178.

Nitrous-Oxide and Ether Anaesthesia

Convulsions

W. B. Cook records convulsions associated with nitrous-oxide ether anaesthesia in a woman, aged 29, who had been under the anaesthetic about an hour and a quarter. When a supravaginal hysterectomy for uterine fibroid was nearly completed she began to have twitching of the eyelids which rapidly spread to the muscles of the face and neck, then to the anus, and finally to the entire body. Respiration was embarrassed and the pulse became weak. The convulsions, which lasted 12 minutes, must be distinguished from ether clonus, or ether rigor, a condition often occurring during the induction and due to lack of oxygen, and soon passing off as the anaesthesia deepens.

L. H. Mousel (1940) also reports the case of a child, aged 6 years, who underwent 5 operations under general anaesthesia with nitrous oxide, oxygen, and ether. Nothing unusual occurred in connexion with the first 3 operations; but 24 hours before the fourth operation the child's temperature was 99.6° F., and at the end of the operation after the anaesthesia became light, muscular twitchings were first noticed round the eyes and general convulsions became severe with deep cyanosis, rapid pulse, and dilated pupils. Six or 7 c.c. of a 2.5 per cent solution of pentothal sodium were injected intravenously and a high concentration of oxygen was given in an oxygen tent; the temperature was 101.4° F. and the pulse 160. Next day the temperature was normal and convalescence was uneventful. Cultures from the nasopharynx gave a growth of a neurotropic strain of streptococcus. A fortnight later a fifth operation was carried out without any convulsion, and nasopharyngeal cultures were negative for streptococci. Review of the literature showed that such convulsions during general anaesthesia, many of which proved fatal, had been reported with increasing frequency during the last 12 years, and had been ascribed to many causes, such as impurities in the ether or in the oxygen, hypoglycaemia, overdosage with atropine, cerebral anaemia, alkalosis, hyperventilation, idiosyncrasy, disturbance of calcium metabolism, anoxaemia, deficiency of CO₂, and over-oxygenation. F. C. Rosenow and R. M. Tovell (1936) recorded the cultivation of a neurotropic strain of streptococcus from each of 5 such cases, and Mousel (1939) reported another case in which a positive cutaneous reaction to a neurotropic anti-serum was also obtained.

Cook, W. B. (1940) *Northw. Med., Seattle*, **39**, 182.

Mousel, L. H. (1939) *Proc. Mayo Clin.*, **14**, 285.

— (1940) *ibid.*, **15**, 33.

Rosenow, E. C., and Tovell, R. M. (1936) *Amer. J. Surg.*, **34**, 474.

Ether Anaesthesia

Convulsions

F. K. Boston describes a case of ether convulsions in a woman of 39 who was undergoing a hysterectomy because of uterine haemorrhage. The patient was in the Trendelenburg position, and a closed-circuit system for absorption of carbon dioxide was used. The convulsion started about 30 minutes after induction. The patient was at once raised to the horizontal position. This eased respiration and decreased cerebral congestion. The re-breathing bag was filled with oxygen alone, and the lungs were inflated with this about 15 times a minute by manual pressure on the bag. After a few inflations the bag was freed from exhaled ether and subsequently refilled with oxygen. The blood calcium was rapidly determined by withdrawing

5 c.cm. of blood from a vein in the arm. The author is of the opinion that the marked anti-convulsive powers of evipan or pentothal sodium should be used in checking the spasms, and recommends the intravenous injection of one of these drugs.

Use of Bulk Ether

E. M. Hediger *et al* report their investigations on the use of bulk ether for surgical anaesthesia. Ether can be transferred from a 25-pound drum, either directly by a funnel or by a copper siphon arrangement, to small emptied anaesthetic cans which can then be stoppered with cork. Such ether in a drum can be kept for at least a month without becoming impure. When less ether is used, the small quarter-pound tins can be filled from 5-pound cans, instead of from 25-pound drums. In this way a considerable saving in the cost of ether can be effected.

Boston, F. K. (1939) *Brit. J. Anaesth.*, **17**, 16.

Hediger, E. M., Chenoweth, M. B., and Gold, H. (1940) *J. Amer. med. Ass.* **114**, 1424.

Vinyl Ether

Convulsions

C. J. M. Dawkins reported 9 cases of convulsions observed in 2,406 anaesthetics with vinesthene (divinyl ether). Four of the cases occurred in a series of in-patient operations, and 5 in a series of 2,210 dental out-patient extractions. In the first group the convulsions occurred towards the end of the operation and were very similar in character to those met with in deep ether anaesthesia, except that each case had an evipan induction, and it is well known that the intravenous injection of a barbiturate will at once abort a case of ether convulsions. A different factor must therefore be present in vinesthene convulsions. In the out-patient group the convulsions occurred after the anaesthetic was concluded. None of the cases in either group had a fatal termination. The cause of these convulsions appears to be quite obscure.

I. K. Boston also reported a case of convulsions following vinesthene anaesthesia. The anaesthetic was given through a Goldman's inhaler to a healthy boy aged 5 years. One 3 c.cm. ampoule was used and 4 teeth were extracted. The anaesthetic proceeded normally, but the child did not recover after the mask had been removed and the teeth extracted. Instead he lay in the chair, apparently in good condition, but responding to no sensory stimuli. This state lasted for about 10 minutes and then a convulsion, which lasted for 25 minutes, began. During it the patient's condition was very poor and only partially relieved by oxygen. Suddenly he passed into a stertorous sleep, his colour became better, and about 1 hour later he recovered consciousness. The condition is very uncommon. The convulsion resembles that sometimes seen under ethyl ether. The only possible contributory factors in this case were constipation of the patient and the fact that some laryngismus occurred during the giving of the anaesthetic.

Boston, F. K. (1940) *Brit. med. J.*, **1**, 929.

Dawkins, C. J. M. (1940) *Brit. med. J.*, **1**, 163.

Ethyl N-Propyl Ether

W. E. Brown studied the anaesthetic properties of ethyl *n*-propyl ether. This is a liquid at ordinary temperature and pressure. It boils at 63.6° C. and has a specific gravity of 0.75. It has a not unpleasant ethereal odour. In anaesthetic concentrations it does not have the more or less suffocating effect of di-ethyl ether. It appears to cause no bronchial secretion or salivation, and it produces no change in arterial tension, and anaesthesia seems easily maintained. Experiments showed that ethyl *n*-propyl ether gave an excellent anaesthesia, had a very unusual safety factor, and was free from unpleasant after-effects. The author considered that the study of this new anaesthetic agent should be continued.

Brown, W. E. (1940) *Canad. med. Ass. J.*, **42**, 370.

Spinal Anaesthesia

Fall in Blood-Pressure

Treatment by parendrine M. D. Altschule and S. Gilman report the results obtained with parendrine (*p*-hydroxyphenylisopropylamine) in correcting the fall of blood-pressure observed in 50 cases of spinal anaesthesia. All the cases were abdominal with the exception of 2 amputations of a lower limb; procaine hydrochloride (novocain) or nupercaine (percaine) were the anaesthetics used. Measurements of pulse rate and blood-pressure were made every 5 minutes; when the latter fell markedly, parendrine was administered in doses of 10 to 20 mg. intramuscularly or 5 to 10 mg. intravenously, or both. The rise in blood-pressure was considered satisfactory if the systolic pressure was maintained above 100. Parendrine has a powerful pressor action due to stimulation of the smooth muscle of the arterial wall and is effective by mouth, intramuscularly, or intravenously. In each of the 50 cases recorded the administration of parendrine was followed by a return of blood-pressure to a satisfactory level. The pressure usually began to rise within 5 minutes after the intramuscular injection of 10 mg. of the drug, if no rise was noted at this time, a second injection was given, the pressure was maintained at a satisfactory level for half an hour to over 2 hours following intramuscular injection. Following intravenous injection the rise was detectable in 2 or 3 minutes and lasted from 20 to 25 minutes. The procedure was standardized as follows: when the systolic pressure falls markedly but not below 50, 10 mg. is given intramuscularly. If no rise occurs within 5 minutes, a second injection of 10 mg. is given intramuscularly. If the systolic pressure falls below 50, 5 mg. is given intravenously. When the systolic pressure has again fallen below 100, usually in 15 to 20 minutes after intravenous injection, 10 mg. is given intramuscularly. Parendrine has certain advantages over other pressor drugs previously used in correcting or preventing the fall in blood-pressure during spinal anaesthesia. Parendrine does not cause cerebral hyperactivity such as is seen following benzedrine or ephedrine. It also differs from epinephrine (adrenaline) or ephedrine in that it has little or no direct stimulating action on the heart, all or most of its action being peripheral. The authors suggest that parendrine might be also useful in the treatment of various types of peripheral vasomotor collapse.

In Abdominal Surgery

R. R. Graham and W. L. Brown stated that spinal anaesthesia has reached a stage where its permanent place is assured. The safety of the procedure is in direct ratio to the experience of the anaesthetist. It must be administered and supervised by a physician specially trained in its use. Nupercaine (percaine), 1 in 1,500, is the agent of choice, being replaced by procaine when conditions prevent its use. Adequate pre-operative sedation is of great value during the operation in preventing nausea and acceleration of the pulse and respiratory rate, as well as lessening the changes in blood-pressure. A severe fall in the systolic blood-pressure can be prevented by the hypodermic injection of ephedrine hydrochloride, $\frac{1}{2}$ grain, immediately before giving the anaesthetic, and serious fluctuations of the systolic pressure can be further controlled by small doses of epine and ephedrine during the operation whenever any fall in pressure commences. Anoxia is prevented by a stream of oxygen run into a tent about the head, formed from the end of the laparotomy sheet. The use of a small No. 22 gauge needle for the spinal puncture reduces to a minimum the leak of spinal fluid from the dural puncture. The prevention of such a leak, in conjunction with the intravenous administration of fluids by the drip method and elevation of the foot of the bed immediately after the operation, has practically eliminated spinal headache. Post-operative over-breathing, with frequent changes in posture, minimize the incidence and seriousness of chest complications.

Altschule, M. D., and Gilman, S. (1939) *New Engl. J. Med.*, **221**, 600.

Graham, R. R., and Brown, W. F. (1939) *Ann. Surg.*, **110**, 863.

Local Anaesthesia

Effect of Adrenaline on the Toxicity of Local Anaesthetics

M. R. Gurd and I. Sachs, of the Nuffield Institute for Medical Research, Oxford, investigated experimentally the effect of adrenaline added in various concentrations

to solutions of cocaine on the toxicity of the latter when injected subcutaneously into white mice. These results are of a preliminary character and mainly concerned with the effect of adrenaline on cocaine, and not of much practical importance, because cocaine is not now used as a subcutaneous anaesthetic. They are, however, of theoretical interest as a necessary step before a study of other anaesthetic drugs, such as procaine, which are of greater practical value. Opinions about the effect of vasoconstrictors on the toxicity of anaesthetics have been conflicting. The following conclusions were reached: (i) The lethality curves of cocaine, alone and in combination with various constant doses of adrenaline, show that doses of 0.2 $\mu\text{g/g}$ (a concentration of 1 in 50,000 of the solution injected) or more of adrenaline cause a substantial increase in the toxicity of cocaine. Doses of 0.118 $\mu\text{g/g}$ (a concentration of 1 in 85,000) or less of adrenaline do not have a significant effect on the toxicity of cocaine. (ii) Doses of 0.2 $\mu\text{g/g}$ (a concentration of 1 in 50,000) or more of adrenaline increase the toxicity of procaine in the same way, and roughly to the same extent, as they do that of cocaine.

Gurd, M. R., and Sachs, I. (1939) *Quart. J. Pharm.*, **12**, 713.

Basal Narcosis

Avertin

Benzedrine for interrupting anaesthesia—Many drugs have been tried in the attempt to overcome the action of avertin. Once the drug has been absorbed into the system it cannot be withdrawn. Recently benzedrine sulphate has been used to interrupt avertin anaesthesia. J. Boyd tested its action in 10 children who had received 0.16 g. of avertin per kilogram of body weight. Supplementary anaesthesia was necessary in 6 cases. They were given 10 mg. of benzedrine sulphate in distilled water intravenously immediately after the operation. One child received only 5 mg. This injection resulted in a reduction in the amount of post-operative sleep. It also led to an earlier return of the superficial reflexes, but it caused severe post-operative vomiting.

Pentothal Sodium

H. S. Ruth *et al.* discuss the uses of pentothal sodium and the reasons for its growing popularity as an intravenous anaesthetic. Among contra-indications to its use are severe anaemia, laryngeal or pharyngeal obstruction, any surgical manipulation interfering with the laryngeal or pharyngeal reflexes, and gross hepatic disease. It should seldom be used for patients under 10 years of age. During its administration it is very important to keep an airway open. The usual maximal dose of 1 g. should seldom be exceeded. Vomiting, nausea, or headaches are rare after this anaesthesia, and there were not any post-operative pulmonary complications among a large number of cases.

Respiratory depression—According to I. B. Mallinson pentothal sodium can produce considerable respiratory depression, especially after heavy premedication or excessive dosage. There are 2 chief ways of correcting respiratory depression severe enough to cause anoxaemia: (i) stimulation of the respiratory centre by drugs injected, or by inhalation of carbon dioxide, (ii) inflation of the lungs with oxygen under pressure by an apparatus designed by the author. It is, however, only when the means to correct the resulting anoxaemia promptly and adequately are lacking that respiratory depression may result in myocardial damage and cardiac failure with consequent collapse and its attendant perils. If such means are available, little fear need be felt of any major complication arising during anaesthesia. Statistics with regard to intravenous anaesthesia, which now exceed 8,000,000 administrations, tend to show that this type of anaesthesia compares favourably with any other form, with the possible exception of gas and oxygen, in respect of mortality. The constant presence of a source of oxygen under controlled pressure during intravenous anaesthesia materially adds to the already excellent margin of safety possessed by this type of anaesthetic.

For reduction of simple fractures—According to P. S. Marcus pentothal is the best anaesthetic for the reduction of simple fractures, because it produces sufficient muscular relaxation, can be continued as long as is necessary, has short induction and emergence times, an adequate margin of safety with few contra-indications,

and there is available a specific therapy for an excess of the agent. During 10 months, pentothal was used for approximately 300 patients who were admitted, diagnosed, X-rayed, treated, and sent home as ambulatory patients. There were no fatalities and only one patient required oxygen therapy and an analeptic for respiratory depression. Vomiting was present in only one case, and in no case did insufficient relaxation occur.

For encephalography. M. J. Nicholson and I. F. Sise found pentothal sodium anaesthesia to be satisfactory for encephalography in 177 cases. The dosage varied according to the case, but the average was 0.85 g. which provided anaesthesia for the introduction of air and the taking of radiographs, a procedure which took 30 to 35 minutes. The minimal dose was 0.3 g. and the maximal 2.0 g. In most cases 1-1.50 gram of atropine sulphate was injected subcutaneously one hour before operation. The advantages of pentothal are as follows. It gives adequate anaesthesia, it overcomes the undesirable reactions, such as headache, nausea, vomiting, pallor, cyanosis, perspiration, chilliness, restlessness, and poor pulse, formerly observed when encephalography was done under local anaesthesia, it obviates the danger of fire and explosion from inflammable anaesthetics in the X-ray room, it provides rapid, smooth, and pleasant induction for patients in the sitting position, and it eliminates the possibility of psychic shock. It is contra-indicated in children under 7 years of age, in hepatic insufficiency, jaundice, and severe renal disease, in patients with increased intracranial pressure with possible medullary compression, and in patients being treated with sulphanilamide.

Sodium Amytal

Effect of benzedrine and paredrine on awakening. A. Myerson *et al.*, who had previously reported that the duration of the narcosis produced by the intravenous administration of sodium amytal was distinctly shortened by the subcutaneous injection of amphetamine (benzedrine) sulphate either before or after the sodium amytal, made a further study of benzedrine given intravenously. At the same time they investigated the effect of another sympathetico-mimetic amine, paredrine (*p*-hydroxyphenyl isopropylamine) hydrobromide, on sodium amytal narcosis. In 19 cases deep sleep was induced by sodium amytal, and immediately after, or within a few minutes, of the injection of this drug, 30 to 40 mg. of benzedrine sulphate were given intravenously through the same needle. In 16 cases clear-cut awakening occurred within 10 minutes, and in the other 3 in 16, 19, and 20 minutes. In 9 cases awakening occurred within 5 minutes. As the effect of the benzedrine wore off, the patients appeared to become drowsy, but were able to walk about, with some complaint of ataxia and giddiness. In 5 cases the two drugs were given simultaneously, the dose of sodium amytal varying between 0.5 and 1.0 g., and the dose of benzedrine sulphate in most cases varying between 20 and 30 mg. intravenously, except in one case in which 14 mg. were given intramuscularly. In no case was either superficial or deep sleep produced, and only slight drowsiness was produced. The speech of all the subjects showed thickness and ataxia. In 10 cases the administration of benzedrine sulphate, 30 mg. intravenously, was followed by that of sodium amytal, usually within 15 minutes, but occasionally as long as half an hour later. In 4 cases deep sleep lasting from 5 to 20 minutes occurred, followed by awakening. In the other 6 cases only drowsiness was evident. Similar experiments were carried out with paredrine and sodium amytal, but it was found that paredrine had no effect on sodium amytal narcosis. This action and the fact that benzedrine causes a rapid and prolonged rise in blood-pressure may be found useful in certain medical or surgical cases in which it seems desirable to overcome severe side reactions of the narcosis produced by the barbiturates, especially respiratory embarrassment and pronounced decrease in blood-pressure.

Boyd, J. (1940) *Brit. med. J.*, **1**, 729.

Mallinson, I. B. (1940) *Brit. med. J.*, **1**, 123.

Marcus, P. S. (1940) *New Engl. J. Med.*, **222**, 137.

Myerson, A., Loman, J., Rinkel, M., and Tesses, M. F. (1939) *New Engl. J. Med.*, **221**, 1015.

Nicholson, M. J., and Sise, I. F. (1940) *New Engl. J. Med.*, **222**, 994.

Ruth, H. S., Tovell, R. M., Milligan, A. D., and Charletoy, D. K. (1939) *J. Amer. med. Ass.*, **113**, 1864.

ANEURYSM

See also B.F.M.P., Vol. I, p. 501, and Surveys and Abstracts 1939, p. 213.

Aneurysm of Aorta

G. Friedlaender analyses 18 cases of aortic aneurysm studied radiologically and clinically, 11 were in males and 7 in females, the average age in 10 males was 50 years, the extremes being 75, in a tabetic who had syphilis 56 years before, and 22 in a congenital syphilitic. The average age of 5 women was 47 years. Radiological examination is by far the most important method of diagnosis. In only 2 of the 18 cases was it possible to make a correct diagnosis from physical signs, though in 3 or 4 more it could at least be suspected. In various statistics the percentage of cases in which syphilitic aortitis and aneurysm will follow has been 10 to 20, and that this estimate is not higher, it is suggested, is because a large number prove fatal from aortitis before an aneurysm can become clinically obvious. Radiology therefore renders diagnosis possible not only in more cases, but earlier, and the interval between the date of recognition of an aneurysm radiologically and the patient's death is longer than that between clinical detection and death. In 2 patients, both alive, the duration was 14 and 20 years. In 22 per cent of the 18 cases the aneurysms had come to a standstill clinically and radiologically. Increase in size of an aneurysm does not always correspond to the deterioration of the clinical state and *vice versa*. Aneurysms of the arch of the aorta may cause quite different and contrary pressure effects on the trachea, those of the first part of the arch push the trachea backwards and may compress it, those of a more distal part and of the junction of the arch with the descending aorta may cause considerable forward dislocation. Well-marked calcification of the aneurysm's wall was present in 4 cases, in 2 of which the disease had come to a complete standstill. Out of the 18 patients 7 had survived for more than 5 years since the aneurysm was detected radiologically. Seven patients were the subjects of aortic incompetence, a complication which has been regarded as a bad prognostic, but the author is of opinion that this is not due to the valvular lesion but to widespread syphilitic vascular disease. The effect of antisyphilitic treatment appears to vary, in some cases it failed to check progress of syphilitic aortitis, in one instance of widespread vascular disease it was probably harmful, in others it was beneficial and in 2 cases the calcification of the aneurysm wall, a conservative process, increased as an apparent result.

C. Frothingham *et al.* report the case of an athletic man, aged 58, who had been under medical observation for 30 years and eventually died after 3 days' illness. There was a sharply-cut transverse rupture of the aorta just above the valves, the illustration of which resembles that due to syphilis of which there was not any evidence. There were also old lacerations and dissecting aneurysms of the abdominal aorta. The aortic valves were structurally normal but incompetent from dilatation of the aorta, an aortic diastolic murmur was heard a year before death. The cause of the aortic changes was idiopathic necrosis of the middle coat of the aorta with resulting loss of elastic and muscular tissue. Haemorrhage into the pericardium gave rise, in the last few days of life, to electrocardiographic changes characteristic of acute coronary obstruction, the mechanism was regarded as external pressure on the coronary vessels, the effect of which was the same as that of internal lesions (thrombosis or endarteritis) of the coronary arteries.

Dissecting Aneurysm

T. East reviewed the clinical features of a dissecting aneurysm and described a case occurring in a woman of 43 years who suffered from a very high blood-pressure and survived for 5 years after the dissection began. The condition is commoner in men and those over the age of 40 years. Most of the patients have a high blood-pressure. The dissection usually starts when the patient is engaged in some physical activity, such as straining at stool. Excruciating pain lasting a few hours or days is usually the first symptom. It may start almost anywhere in the trunk and then spreads. If epigastric, it may be diagnosed from surgical catastrophes by the absence of rigidity. Shock, collapse, and vomiting are common. Neighbouring structures such as the oesophagus and carotid arteries may be pressed on by the extravasated

blood. Systolic and/or diastolic murmurs frequently develop over the aortic valves. The reflux is relative due to distension of the aorta interfering with closure of the aortic valves. A characteristic result of a dissecting aneurysm is interference with the peripheral circulation to the limbs leading to a loss of pulsation. The pulses may return after a time, or the limbs, especially the legs, may become numb and lose sensation. Leucocytosis is usually present, and jaundice from absorption of blood and a slight fever may occur. X-ray examination shows the dilatation of the aorta and pulsation may be present. Most of the cases are fatal in a day or two, usually from rupture into the left pleural or pericardial sacs. If the aneurysm does not rupture, healing may occur, absolute rest with full doses of morphine being essential.

Dissecting Aneurysm in Adolescent

E. Gardner *et al.* describe a very extensive dissecting aneurysm occurring in a boy of 15 years. Dissection was present in the aorta and its main branches down to the popliteal artery on the left and the posterior tibial on the right. The pulmonary artery, its right main branch, and the right coronary artery were also dissected. Pathological examination showed no gross lesions in the walls of the vessels but degeneration of the media was thought to be the probable underlying cause. Most of the aorta, in which the aneurysm probably started, was disintegrated and it was therefore impossible to find any causal lesion there. The heart was healthy. The symptoms pointed to the abdominal aorta being the seat of primary rupture. The stress of defaecation was probably the immediate cause. The patient had a cold and complained of pain in the back. Two days later he was seized with violent pain after defaecation and later agonizing pain and cramp developed in both legs. He was relieved by hot baths but developed abdominal rigidity and respiratory distress. The next day he died suddenly after an attack of severe pain rising up from the abdomen into the chest. The authors believe that dissecting aneurysm is probably a commoner cause of death than is supposed and some cases described as coronary thrombosis may, in reality, be due to this condition.

East, I. (1939) *Lancet*, **2**, 1017

Friedlaender, G. (1940) *Brit. J. Radiol.*, N. S., **13**, 109

Frothingham, C., Sanderson, E., and Hazard, J. B. (1939) *Trans. Roy. Amer. Phys.*, **54**, 333

Gardner, E., Galbraith, A. J., and Hardwick, S. W. (1939) *Lancet*, **2**, 1019

Aneurysm of Common Carotid or Innominate Artery

Differential Diagnosis

Kinked carotid artery simulating aneurysm—J. Parkinson *et al.*, on the basis of 47 collected cases and of a review of other recorded examples, describe a condition imitating aneurysm of the innominate or the right common carotid artery, the latter being shown to be much rarer than is often stated and, when it does occur, to be only an extension from an aneurysm of the innominate artery. The 47 cases of this kinked condition of the right common carotid artery are divided into 3 groups: (i) 40 with arterial sclerosis and hypertension? 30 with a blood-pressure above 160/95 mm. Hg. and 24 above 200 mm. Hg.; 10 showed arteriosclerosis alone. All were women between the ages of 41 and 79 years, the average being 59 years. In half of the cases there was evidence of thickening and tortuosity of the radial and brachial arteries; there were not any signs of syphilis and, among 22 in which a Wassermann reaction was recorded, one only was positive. The cardiographic feature was left axis-deviation, as would be expected from the frequency of associated hypertension. The prognosis depends on the cardiovascular disease and not on the kinked carotid, and survivals for 5 to 25 years are on record. The typical case is that of a middle-aged or elderly woman, often stout, kyphotic and scoliotic, with a pulsating swelling visible and palpable behind the sternal head of the right sternocleidomastoid muscle. The vascular condition of tortuosity and general dilatation is correlated with hypertension, and the dynamic factor is important, for the bulge seen in life usually disappears after death. (ii) In 4 cases, including one reported by Corrigan in 1832, there was aortic incompetence, and (iii) in 3 cases there was coarctation of the aorta. In a fourth group are quoted examples of other

congenital vascular abnormalities, such as tortuosity of the internal carotid artery in the young, which may be unilateral or bilateral. Reference is also made to Kelly's review of 150 cases, among which were 21 over the age of 60 believed to be arteriosclerotic, and occurring mainly in women.

Kelly, A. B. (1924) *Proc. R. Soc. Med.*, **17** (Sect. Laryngol.), 1.

Parkinson, J., Bedford, D. I., and Almond, S. (1939) *Brit. Heart J.*, **1**, 345.

Congenital Intracerebral Aneurysm

K. Hermann and A. R. MacGregor record a case in a boy, aged 4½ years, of an unusual form of congenital aneurysm, namely intracerebral, thus differing from the well-known congenital aneurysms of the arteries of the circle of Willis at the base of the brain, which rupture into the subarachnoid space. The authors have been unable to find a recorded case of a verified congenital intracerebral aneurysm, with or without rupture and haemorrhage. This boy, while playing, suddenly complained of pain in the left ear, rapidly became unconscious and died 15 hours after the onset. Respiration had stopped before the pulse, and accordingly artificial respiration was maintained for several hours after insertion of a tracheal tube, and exploratory cranial perforations were made in both parietal regions; there was no blood on the surface of the brain, which was very tense, but blood was drawn off from both lateral ventricles by a cannula. The necropsy, confined to the head, showed a blood-containing cavity about 4 cm. in diameter, immediately anterior and lateral to the anterior horn of the left lateral ventricle, into which rupture had occurred. In the wall of this cavity in the left frontal lobe there was a ruptured oval aneurysm, 6 mm. in its longest diameter, which arose from a bifurcation of one of the deep branches of the anterior cerebral artery. The wall of this aneurysm showed in parts two different changes, namely (i) thinning due to disappearance of the muscular media, and elastic fibres, and evidence of congenital hypoplasia and aneurysm, and (ii) fibrous thickening due to organization of a small haemorrhage at a date considerably earlier than that of the fatal ruptures. Another smaller and unruptured aneurysm was found microscopically in the wall of the cavity; the muscular tissue of the parent artery ended abruptly at the neck of this aneurysmal sac.

Hermann, K., and MacGregor, A. R. (1940) *Brit. med. J.*, **1**, 523.

ANGINA PECTORIS AND CORONARY THROMBOSIS

See also B.F.M.P., Vol. I, p. 547. Cumulative Supplement Key No. 62 and Surveys and Abstracts 1939, p. 215.

Angina Pectoris

etiology

W. J. Kerr *et al.* describe angina pectoris in patients with obesity, protuberant pendulous abdomen, exaggerated spinal curves, florid complexion and poor posture. When at rest in the reclining position these patients are 'for all practical purposes compatible with normal subjects in the same position, it is only when they assume the erect position and begin to exert themselves that their functional incapacities become apparent. It is argued that relative anoxaemia in some part of the myocardium or the base of the aorta initiates the pain, and it is shown that faulty filling of the heart leads to an inadequate output of blood during systole, and it is assumed that this results in an insufficient supply of oxygen to the vulnerable tissues. The chief disturbance in nearly all these patients is associated with faulty movements of the diaphragm, and thus the important function of the diaphragm in facilitating the return of blood to the heart is impaired. These considerations bear on the treatment suggested by the authors (see p. 46). In the discussion which followed this paper G. Canby Robinson mentioned that 25 years ago George Draper and he wrote a paper, never published, describing the benefit due to a binder in cardiac failure and employing the term 'pulse deficit', which was first published, with acknowledgements, in 1914 by Walter James and Hart.

Thyroid dysfunction.—I. C. Mussio-Fournier and I. T. Fischer state that 'besides

the type of angina pectoris caused by cardio-vascular disease, there is also a type of angina pectoris of hormonal origin, in which the thyroid is of predominant importance. Myxoedema may be combined with angina pectoris, both conditions disappearing under thyroid substitution therapy. There are cases, however, in which thyroid therapy will aggravate the angina whilst relieving the myxoedema. The authors describe several cases and stress the difficulty of determining the pathogenesis. They presume a constitutional cardio-vascular weakness in which the thyroidal dyscrasia causes or accentuates organic modifications such as sclerosis, mucous infiltrations, and dilatations. The myxoedema, as a general disease, causes a diminution of the minute-volume and an asphyxia of the cardiac muscle which provokes the anginal pain. There is also an angina pectoris combined with hyperthyroidism (Graves's disease, toxic adenomatous goitre, or mixed forms). Hyperthyroidism by its very nature affects the circulatory system, and the increased basal metabolism means a super-charge upon the heart muscle which will cause angina pectoris. Angina pectoris is no contra-indication to thyroidectomy.

Clinical Picture

I. P. Scarlett analysed 100 cases of angina pectoris. The onset occurred between the ages of 32 and 74 years in 85 men and 15 women; the average age at onset was 57 in both sexes, and at death in 35 men 64 years and in 5 women 56 years. The average survival after the onset in the 40 fatal cases was 3½ years, and in the remaining living patients 4·6 years, one patient surviving for 13 years. Hypertension (above 150/96 mm. Hg.) was found in 37 patients, 18 among those who died and 19 of the 60 living; the incidence of hypertension was much higher in women, 12 out of 15 compared with 25 out of 85 men. A normal electrocardiogram was present in 25 patients and carried with it a better prognosis. Half the deaths were sudden. In 92 patients the pain was substernal or epigastric, and the radiation spread to both arms in 22 patients, to the left arm in 18, right arm in 3, neck and jaws in 13, and back in 2. In 42 patients there was not any radiation.

Pathology and Pathogenesis of Anginal Pain

Sir James Mackenzie, who died in January 1925, at the age of 72, left directions that after his death his heart should be examined in order to ascertain what information it furnished concerning his symptoms. This was carried out by Professor David Waterston and other friends of Mackenzie. Dr. James Orr, who saw him in attacks of angina at St. Andrews, summarizes the medical history. The first evidence of real cardiac involvement was caused by running 300 to 400 yards when 47 years old, and a tracing taken by himself showed auricular fibrillation. The first severe attack of cardiac pain occurred at the age of 55 when he was resting, and the morbid changes found after death in the heart suggested coronary thrombosis then, and numerous small thromboses at different times. The presence of numerous small blood vessels on the surface points to there having been an opening up of small vessels and the establishment of at least a partial anastomotic pathway for the supply of blood to the areas most severely impaired by the attacks of thrombosis (T. Lewis). Both coronary arteries and their branches showed extensive and far-advanced sclerosis in the form of patchy thickenings of their walls, which in some places diminished and practically obliterated the lumen. The histological changes in the heart and the coronary arteries are described in detail with a number of figures (D. I. Cappell). The valves of the heart were efficient, the impairment being entirely in the myocardium and due to the lesions in the coronary arteries.

Treatment—Medical

Modifying effect of certain drugs on pain. R. Levy *et al.* investigated the modifying effect of certain drugs on the time of appearance of cardiac pain caused by induced anaemia in 10 patients (9 males and 1 female, with an average age of 59 years) with coronary sclerosis, and subject to spontaneous attacks of anginal pain relieved by nitroglycerin. An apparatus was used to induce oxygen want in a patient by breathing a mixture of 10 per cent oxygen and 90 per cent nitrogen for 20 minutes. Nine of the 10 patients experienced pain during the test. The results, based on 86 tests and the measurements of 739 electrocardiograms, were as follows: aminophyllin, injected intravenously, caused prolongation in the time of the appearance

of the pain by 63 per cent. There was less deviation of the RS-T junctions, and the T-waves were modified significantly in 7. Nitroglycerin caused a prolongation of 51 per cent in the time of the appearance of pain, there was less deviation of the RS-T junctions in 6 out of 9 cases, and the T-waves were modified significantly in 6. Aminophyllin by mouth, 4 times daily for a week, caused a prolongation of 26 per cent in the time of the appearance of the pain. There was less deviation of the RS-T junctions in 4 out of 10 cases, and the T-waves were modified significantly in 7. Digitalis caused the usual changes in the RS-T junctions and T-waves in all controls. With the anoxaemia test the time of the appearance of pain was shortened by 9 per cent. Lactose and erythrol tetranitrate did not significantly prolong the time interval of the pain. It was concluded that nitroglycerin relieves anginal pain by dilating the coronary arteries and not by lowering the general systemic blood-pressure, and that erythrol tetranitrate, although apparently causing slight dilatation of the coronary arteries, is not effective in lessening the tendency to anginal pain.

Treatment surgical. At a joint meeting of the sections of Medicine and Surgery of the Royal Society of Medicine, London, the present position of the surgical treatment of angina pectoris was reviewed. G. Bourne insisted on the difficulty of determining the cause of cardiac pain, and pointed out that the fuller the available information the higher is the percentage of patients diagnosed as suffering from coronary disease, and that severe angina of effort indicates coronary disease with living muscular fibres distally which are periodically starved of their blood supply. Surgical measures are employed in angina of effort for the relief of pain and to effect revascularization. (i) T. C. White injected alcohol into the upper 5 dorsal ganglia on the left side with much success, but the procedure may be attended by minor accidents such as partial pneumothorax and local pleurisy, and in a few cases by alcoholic neuritis. Among about 400 cases of angina of effort under Bourne's observation, 15 with very severe pain were submitted to thyroidectomy and 10 did well. The indications for thyroidectomy are a correct diagnosis and severe pain without improvement, the contra-indications are adiposity, and a progressive cardiac lesion. The patient should remain in bed for 3 to 5 weeks after the operation, and thyroid should not be given until slight signs of myxoedema, such as increase of weight, chilliness, and lethargy, appear. (ii) Revascularization. Of 5 such operations at St. Bartholomew's Hospital 1 patient died immediately after it was performed, while another died 16 months after, having in the interval become increasingly dyspnoeic but free from pain. The necropsy did not show revascularization. The other 3 patients were much improved.

Cardio-omentopexy. J. Paterson Ross places muscle grafting or omental grafting first among the operations for the relief of angina, the function of the omentum in providing a blood supply to infarcted portions of abdominal viscera is well known, and cardio-omentopexy has a sound theoretical foundation. It is, however, a more formidable operation than either thyroidectomy or sympathectomy. Total thyroidectomy is recommended, and a technique in order to avoid with certainty damage to the recurrent laryngeal nerve is described. The suggestion that the effect of thyroidectomy is due to section of the sympathetic nerves is contested. It is important to consider the influence of the thyroid secretion, though it is quite possible that thyroxine may not be directly responsible for the pain, it may be that its effect comes from sensitization of the tissues to circulating adrenaline. Sympathectomy is beneficial because, in the division of the sympathetic, the visceral sensory fibres accompanying them are also cut. Stellate ganglionectomy will block a large proportion of the afferent nerve fibres from the heart, but, as pain fibres enter the spinal cord along the white ram of the upper 4 or 5 thoracic nerves, complete sensory denervation involves a very extensive operation. As injection of alcohol has the drawback that it may cause intercostal neuritis, excision of the sympathetic is recommended whenever the patient's condition allows this. The majority of patients with angina stand the strain of operation surprisingly well.

A. Dickson Wright regards revascularization as attractive in theory but open to the objections that (i) throughout the body it is impossible to induce any organ to take up a new blood supply when its own is intact, and after all the myocardium is only short of blood during infarction, (ii) after infarction no amount of revascularization can restore muscle fibres, and (iii) the high mortality of the operation, the only condition in which this operation might be justified is in familial coronary

thrombophilia in which all the male members die from coronary thrombosis early in the fifth decade of life

H F Mansell regards as the ideal indication for cardio-omentopexy specific aortitis with narrowing of the coronary orifices, and agrees that the operation is seldom needed in cardiac infarction. Out of 15 patients treated by cardio-omentopexy 7 have died, and in 4 of these vascular channels were found at necropsy between the omentum and the left ventricle. In another patient who had recovered sufficiently to go back to work but died suddenly, the graft was lying free in the left pleural cavity.

J W Strieder *et al* performed cardio-omentopexy in 2 cases of coronary disease with angina pectoris. There was no operative mortality in these 2 cases. In one case great relief of pain followed the operation, and the patient required no drugs and showed a marked improvement in exercise tolerance. He died, however, 6 months later as the result of operation for a diaphragmatic hernia. The second case was alive 13 months after operation, he still had pain, though this was less severe, required some medication, and had a greatly improved 'exercise' tolerance. The authors insisted that the patients should be under 60 years of age and not obese, and that there should be no serious complications in other organs. Patients with marked hypertension and cardiac enlargement were considered unsuitable. Many more patients must be operated on before any sweeping conclusions may be drawn, but the principle of revascularization appears to be sound.

Section of left sympathetic -- For the relief of angina pectoris R B Rancy describes an operation which acts, not by establishing anaesthesia, but by the prevention of spasm of the coronary arteries. The spasm is ascribed to the abnormal action of sympathetic impulses producing morbid changes at the myoneural junction. The operation consists of section of the left sympathetic chain between the 5th and 6th dorsal ganglia and division of the rami communicantes from the second to the fifth ganglia. The efferent pathway is therefore almost entirely uninterrupted and Horner's syndrome is not produced. Eleven patients thus treated obtained complete relief from their attacks, there was no fatality.

Elastic supporting belt - In the angina of their obese patients, W J Kerr *et al* found that an elastic supporting belt was of great value in restoring the function of the diaphragm, and thus improving the circulatory conditions and the filling of the heart. This abdominal support should be adjusted to secure the most complete movements of the diaphragm, preferably under the fluoroscope. It is not worn in bed, but a simple rubber or other elastic belt may be worn when a shower-bath is taken.

Bourne, G (1940) *Proc R Soc Med*, **33**, 535.

Kerr, W J, Cannon, E F, and Lagen, J B. (1939) *Trans Ass. Amer. Phys.*, **54**, 225.

Levy, R., Bruenn, H G, and Williams, N E (1939) *Trans. Ass. Amer. Phys.*, **54**, 244.

Mansell, H E (1940) *Proc R Soc Med*, **33**, 542.

Mussio-Fournier, J C, and Fischer, J T (1940) *Pr méd*, **48**, 363.

Rancy, R. B (1939) *J Amer med Ass*, **113**, 1619.

Robinson, G C (1939) *Trans Ass. Amer. Phys.*, **54**, 232.

Ross, J P (1940) *Proc R. Soc. Med.*, **33**, 538.

Scarlett, L P (1940) *Canad med Ass J*, **42**, 34.

Strieder, J. W., Clute, H M., and Graybiel, A. (1940) *New Engl J Med.*, **222**, 41.

Waterston, D (1939) *Brit Heart J*, **1**, 237.

White, J C (1940) *Proc R Soc Med*, **33**, 536.

Wright, A D. (1940) *Proc R. Soc. Med.*, **33**, 540.

Coronary Thrombosis

Clinical Picture

Relation to pathological findings - H. I. Blumgart *et al* made a joint investigation of 125 consecutive cases in order to gain further insight into the relationship of the

clinical manifestations of angina pectoris, coronary thrombosis, myocardial infarction, and congestive heart failure to the pathological findings observed in the coronary arteries and the heart muscle. In 30 cases, representing all those patients with clinical evidence of cardiac pain or congestive failure or with anatomical evidence of coronary occlusion, a careful study was made, and the findings compared with those in the other cases of the series.

It was found that, in normal hearts, intercoronary anastomoses larger than 40 micra in diameter do not occur. In normal hearts there are anastomotic communications, measuring less than approximately 40 micra between the coronary arteries; the presence of these can be shown by the injection of watery solutions. Obstruction to normal coronary arterial blood flow by arteriosclerotic narrowing or occlusion regularly results in the development of intercoronary anastomoses measuring 40 to 200 micra in diameter. Anastomotic circulation therefore develops only when and where it is needed. The development of such anastomoses is not related to age. Such anastomotic circulation may so well compensate for occlusion or marked narrowing of a major coronary artery that the blood supply to the heart remains adequate for the ordinary activities of life. When the narrowing or occlusion progresses so far that the coronary circulation is insufficient to meet the needs of the heart during the periods of increased work, myocardial anoxaemia results. In 10 out of 12 cases in which uncomplicated angina pectoris was the primary condition, there were old complete occlusions of at least 2 main coronary arteries. Recent or old coronary occlusions were found in the absence of angina pectoris in 13 out of 125 cases. Only 12 main coronary arteries had been completely occluded before the final illness in these 13 cases, which was in contrast to the fact that in the 12 cases of angina pectoris 25 main arteries were occluded. In 5 cases of angina pectoris complicated by antecedent or coincident congestive failure or by valvular disease, there were relatively few occluded arteries. In these cases angina pectoris and congestive failure were caused chiefly by the greatly increased load on the heart.

With regard to congestive failure in coronary disease or angina pectoris, the results of the study suggested that constantly undernourished areas in hearts which are the seat of coronary arteriosclerosis, when subjected to still greater anoxaemia, as from exertion or emotion, undergo focal necrosis and a diffuse fibrosis. The latter leads to myocardial weakness and congestive failure. A comparative study of the clinical manifestations of coronary thrombosis and of myocardial infarction forces the conclusion that coronary thrombosis and occlusion *per se* do not necessarily produce any clinical manifestations. If an occlusion occurs gradually with the development of an anastomotic circulation, no symptoms or signs will be produced, and no myocardial lesions will be demonstrable. The syndrome, 'coronary occlusion', consisting of prolonged substernal oppression or pain, a fall in blood-pressure, pallor, and other manifestations of shock, and accompanied by electrocardiographic changes, fever, leucocytosis, and increased sedimentation rate really signifies myocardial infarction, and should be so termed. Attacks of severe prolonged pain, associated at times with collapse, evidently result from prolonged insufficiency of the blood supply to the myocardium and consequent anoxia. This 'coronary failure' may occur with or without simultaneous, or immediately preceding, coronary thrombosis. If such 'coronary failure' is sufficiently prolonged myocardial infarction results. In some cases this may be obviated if the demands on the myocardium are quickly reduced by rest in bed, sedatives, or the control of rapid ventricular rates. Sufficient collateral blood flow may be available to satisfy the thus lowered cardiac requirements, and permit recovery of the anoxaemic fibrosis. The duration of pain in such cases of coronary failure may be longer than that commonly seen in angina pectoris, but the clinical manifestations characteristic of myocardial infarction are not found. Although myocardial infarction may occur with or without simultaneous, or immediately preceding, coronary thrombosis or occlusion, the clinical diagnosis of myocardial infarction caused by acute coronary thrombosis would seem to be justified when the symptoms and signs of infarction occur under certain circumstances. The site of an infarct in the heart does not necessarily bear a relationship to the location of occlusion in the coronary arteries. The clinical results of coronary occlusion are significantly influenced by the original pattern of the coronary arteries in any given heart. In some cases in which the coronary blood flow was already reduced, and presumably slowed, the sudden fall

in blood-pressure which accompanied post-operative shock evidently led to further stagnation anoxaemia, and the deposition of multiple coronary arteriosclerosis was emphasized. It was concluded that death occurs whenever a sufficiently large area of the myocardium undergoes ischaemia, with or without necrosis, or when, because of ischaemia, asystole, ventricular fibrillation, or congestive failure occurs. Anoxia, necrosis, infarction, and fibrosis of the myocardium occur whenever there is a discrepancy between the nutritional requirements of the heart muscle and the factors governing the nutritional supply.

Prognosis

W. H. Lewis reports the case of a man who, at the age of 43, had an attack of coronary thrombosis. After careful treatment, he was able to resume his business career, and subsequently carried out activities beyond those advised, or even considered possible. Thus he paid business visits to Europe, flew at various altitudes up to 15,000 feet, even piloting a plane himself, danced, swam, and skied each winter at altitudes up to 10,000 feet, without apparent detriment. Six years later he appeared to be in good health.

Myocardial Infarction

Rate of healing—G. K. Mallory *et al.* investigated 72 cases of myocardial infarction at necropsy, to determine the rate of healing of the infarcts. The average age of the patients was 59, and 74 per cent were males. In practically all cases a generalized arteriosclerosis of the coronary artery accompanied the occlusion. Cardiac rupture had occurred in 8 cases, and diabetes was present in 9. The preponderating areas affected were the apex of the left ventricle itself or the apex and the interventricular septum. The first effect of an infarction is necrosis of the muscle fibres, which may be accompanied by some focal haemorrhage, and is constantly followed by a polymorphonuclear infiltration. At the end of 5 or 6 weeks the necrosed muscle has been replaced by connective tissue. From the twelfth day onwards, the formation of collagen from the connective tissue increases its production, reaching a maximum at the end of 3 months. The replacement by connective tissue leads to increasing zones of red tissue surrounding paler areas of necrosis. Ultimately this granulation tissue becomes paler, and the end result of the infarct is the formation of a pale fibrous scar. The authors are of the opinion that the age of an infarct cannot be judged with histological accuracy after the first 3 weeks, and that small infarcts require 5, and large infarcts at least 8 or 9, weeks for complete healing. In the rapidity with which this latter process is carried out the condition of the remaining myocardial circulation is highly important. Rupture of the heart occurred at any time between the first and twelfth days.

Blumgart, H. I., Schlesinger, M. J., and Davis, D. (1940) *Amer. Heart J.*, **19**, 1.

Lewis, W. H., Jr. (1940) *J. Amer. med. Ass.*, **114**, 484.

Mallory, G. K., White, P. D., and Salcedo-Salgar, I. (1939) *Amer. Heart J.*, **18**, 647.

ANGIOMA

See also B. I. M. P., Vol. I, p. 577, Cumulative Supplement, Key No. 64, and Surveys and Abstracts 1939, p. 218.

Treatment

Radiation Therapy

Radium—B. L. Feuerstein stated that naevus flammeus, or port-wine stain, is extremely resistant to radium therapy. While small lesions can be eradicated by unfiltered radium, the unattractive scarring left, and the frequency of atrophy and telangiectasis, contra-indicate radium therapy. On the other hand radium therapy is highly effective in naevus vasculosus, or strawberry mark. Even large lesions can be eradicated with practically no scarring. No sequelae, local or general, occur.

R. Paterson and M. C. Tod reported on the use of radium in 150 children with angiomas. The technique of treatment consisted of repeated low doses, the authors

suggesting 1,500 r every 2 months. In 129 cases the angiomas completely disappeared. If dosage is carefully estimated, and treatment not continued for too long a period in cases in which the tumour is unusually resistant, a good cosmetic result without damage to the skin is generally obtainable.

Feuerstein, R. L. (1940) *Miss. J. all. med. J.*, **62**, 77.

Paterson, R., and Tod, M. C. (1939) *Amer. J. Roentgenol.*, **42**, 726.

Port-Wine Birthmarks

Treatment

Grenz rays. C. White employed Grenz rays in 8 cases of port-wine birthmarks in adults. Employing treatments at fortnightly intervals, extending over 3 to 9 months, he found that the lesions showed marked bleaching. The author pointed out that until now, there has been no form of treatment free from danger in capillary birthmarks of this type.

White, C. (1939) *Illinois med. J.* **76**, 449.

ANKYLOSTOMIASIS OR HOOKWORM DISEASE

See also B.E.M.P., Vol. I, p. 587. Cumulative Supplement, Key No. 66. and Surveys and Abstracts 1939, p. 218.

Clinical Picture

Nervous Complications

H. Hoff and J. A. Shaby discuss the nervous complications of ankylostomiasis on the basis of 3 cases, which all showed symptoms of subacute combined degeneration of the cord, but without achlorhydria or pernicious anaemia, though with a high degree of secondary anaemia due apparently to infestation with *Ankylostoma duodenale*. A good recovery followed massive doses of iron, vitamin B and liver extract in 2 patients, but in the other patient it was not so complete. Later, carbon tetrachloride was given to remove the parasite.

Hoff, H., and Shaby, J. A. (1939) *J. trop. Med. (Hyg.)*, **42**, 360.

Treatment

Iron and Blood Transfusion for Anaemia

Azmy Pasha and A. F. Zanaty investigated iron and blood transfusion therapy in 20 cases of ankylostoma anaemia, biopsy of the bone marrow being performed before and after both methods of treatment and the blood examined at frequent intervals during the treatment. The patients were divided into 2 groups, (i) those receiving iron only, and (ii) those receiving small transfusions of blood, when these were effective, iron was given and after it had produced its full effect small blood transfusions were given again. In the first group the iron was absorbed and used in spite of the presence of the worms. In the second group transfusions had a temporary value both in the presence and after the expulsion of the worms. After iron therapy the transfusions gave a good response. The haemoglobin rose even higher, the first transfusion producing the optimal effect, the blood and bone marrow in these cases showing a similar picture to that of idiopathic hypochromic anaemia. There was general hyperplasia with marked erythropoiesis. In the light of this similarity, it is suggested that small blood transfusions as well as iron might be used with advantage in the treatment of idiopathic hypochromic anaemia.

Azmy, S., and Zanaty, A. F. (1939) *J. trop. Med. (Hyg.)*, **42**, 263.

ANTENATAL CARE

See also B.E.M.P., Vol. I, p. 601, Cumulative Supplement, Key No. 68, and Surveys and Abstracts 1939, pp. 29 and 219.

Hygiene of Pregnancy

Anaemias of Pregnancy

Effect of iron and diet. F. H. Bethell *et al.* investigated the influence of iron and

diet on the blood of 158 pregnant women. Of these 54 per cent were found to be anaemic. Haemoglobin below 10.0 g. per 100 c.c.m. and red-cell counts of less than 3,500,000 per c.c.m. are pathological. The first is due to deficient iron and the second to deficient protein. Both may occur together. During pregnancy 50 g. of animal protein daily is recommended, but in severe forms of anaemia 1.5 g. per kilo of body weight may be necessary. Inorganic ferrous preparations were found the most suitable for the treatment of anaemia in pregnancy. It was suggested that this should be given as a routine throughout pregnancy as iron is of benefit in this condition and slight degrees of anaemia are difficult to detect.

Bethell, F. H., Gardiner, S. H., and MacKinnon, I. (1939) *Ann intern Med.*, **13**, 91.

ANTHRACOSIS

See also B. I. M. P., Vol. I, p. 621.

Clinical Picture

Cardiovascular System

J. I. Gueting and R. Chart found, on examining 25 miners, that 16 of them had anthracosilicosis without pulmonary tuberculosis, and that 9 had, in addition, moderate or severe pulmonary tuberculosis. Electrocardiograms showed myocardial damage in most of the cases and 2 of them had enlarged hearts. Polycythaemia and reduction in vital capacity often occurred, but the venous pressure and circulation time were within normal limits in all cases. The ages of the men ranged from 36 to 67 years and they had been miners from 3 to 40 years.

Gueting, J. I. and Chart, R. (1939) *J. Amer. med. Ass.*, **113**, 574.

ANTHRAX

See also B. I. M. P., Vol. I, p. 629, and Cumulative Supplement, Key No. 70.

Clinical Picture

Anthrax Meningitis

H. H. Stewart records the case of a woman, aged 32, with a primary lesion on the lower lip, who died after less than 30 hours' illness with a temperature of 103° F. and unconsciousness. Lumbar puncture withdrew turbid fluid containing anthrax bacilli, but not blood-stained. There was not a necropsy. This is a very rare occurrence in anthrax—a haemorrhagic meningitis has been recorded.

Stewart, H. H. (1939) *Uster med. J.*, **8**, 252.

Treatment

Sulphonamide Compounds in Experimental Anthrax

J. C. Cruickshank stated that, while treatment of anthrax with immune serum and arsenicals was of some value, the mortality of the disease treated thus remained very high. To find the effect of chemotherapy on this disease he treated 5 groups of experimentally-infected mice. One group was used as a control and the other 4 received sulphanilamide by mouth, sulphanilamide subcutaneously, sulphapyridine by mouth, and sulphapyridine subcutaneously respectively. Both drugs delayed death from anthrax, though all the mice died. Of the two drugs sulphapyridine was the more effective. By giving large doses of sulphapyridine it was possible to get 11 per cent of survivors if it were given by mouth and 9 per cent if given by subcutaneous injection. Tryparsamide was given by mouth to another group of mice and triparsamide and sulphapyridine to a third group. It was found that triparsamide was without action and did not enhance the effect of the sulphapyridine. Neoarsphenamine given with sulphapyridine was concluded to have an insignificant effect on the survival-rate. It was suggested that sulphapyridine might be of value in the treatment of anthrax lesions in man.

H. B. May and S. C. Buck also experimented with mice infected with anthrax to determine whether drugs of the sulphanilamide class had any effect on the disease and whether they exerted any synergic action with the antiserum. They found that sulphanilamide, a sulphone compound, and sulphapyridine delayed death in the mice. Sulphapyridine was the most efficacious drug in this respect but none of them reduced the mortality-rate from the disease. An anti-anthrax serum prepared from rabbits was found to protect mice and its protective action was increased when sulphapyridine was given with it.

Cruckshank, J. C. (1939) *Lancet*, **2**, 681.

May, H. B., and Buck, S. C. (1939) *Lancet*, **2**, 685.

ANUS DISASI S

See also B. I. M. P., Vol. I, p. 643, Cumulative Supplement, Key No. 71, and Surveys and Abstracts 1939, p. 220.

Pruritus Ani

Treatment

Tattooing with mercury sulphide. R. Furell *et al.* treated 22 cases of pruritus ani by tattooing with mercury sulphide. They employed an electric tattooing machine (3,000 vibrations per minute) with needle handles containing 6 to 20 needles in a single row and protruding 2 to 3 mm. A paste of mercury sulphide in sterile distilled water was used. Infiltration anaesthesia with 0.5 to 1 per cent procaine hydrochloride was employed. The results obtained were so satisfactory that continuation of this treatment was justified. In one case a recurrence of the pruritus of 4 days' duration, disappeared spontaneously.

Furell, R., Buda, A. M., and Marino, A. W. M. (1940) *Arch. Derm. Syph.*, N. Y., **41**, 521.

APOPLEXY

See also B. F. M. P., Vol. I, p. 712.

Prognosis

H. P. Newbill draws the following conclusions from necropsies on 296 persons found dead. It is exceptional rather than the rule for death to occur within 2 hours of cerebro-vascular accidents, in such accidents haemorrhage is more likely to be responsible for death within 24 hours of the onset of symptoms, whereas thrombosis is the commoner in patients surviving for more than a month. The average survival period after thrombosis is approximately 15 times as long as that after haemorrhage or embolism. In cases of thrombosis particularly there was a distinct difference in the survival periods of the white and negro races, which were 105.5 and 64.8 days respectively; there was a similar difference between males and females, namely 57.3 and 129.1 days respectively. In apoplexy occurring between the ages of 21 and 60 the average survival period was one month longer, whereas below 21 and above 60 years of age death generally occurred within one month. The longest survival period was found in the 30-40 group in which it averaged 141 days.

Newbill, H. P. (1940) *J. Amer. med. Ass.*, **114**, 236.

APPENDICITIS

See also B. F. M. P., Vol. I, p. 729, Surveys and Abstracts 1939, p. 221, and p. 12 of this volume.

Aetiology

Neurogenic Appendicitis

H. Bohn described a form of appendicitis which he called neurogenic appendicitis, this was a form of chronic enteritis with an endocrino-neurological basis. The author claimed that appendicitis is often elicited by neuro-muscular dysfunction, basing his assertion on the histological appearances of appendices. In these he invariably found marked hypertrophy of the nervous filaments, and from this he

concluded that the pain simulating acute exacerbation of the disease is due to a neuro-endocrine dysfunction. The treatment of this condition should not therefore be entirely surgical.

Bohn, H. (1939) *Bohn's Beiträge zur klinischen Chirurgie*, **170**, 24

Differential Diagnosis

Pain due to Ovulation

D. J. McSweeney and F. O. Wood report on 257 cases of pain due to ovulation, and analyse its sequelae. The main difficulty is the differential diagnosis from appendicitis. The symptoms are generally more severe the closer the attacks are to the onset of the next period. Appendicitis and pain resulting from ovulation may exist simultaneously. Most cases of ruptured corpus haemorrhagicum can, if definitely diagnosed, be treated without operation, but persistent bleeding may necessitate surgical intervention. It is suggested that when the milder forms of appendicitis are suspected in women and diagnosis is not absolutely certain, a midline instead of a right-rectus or McBurney's incision should be made in order to simplify exploration of the pelvis.

McSweeney, D. J., and Wood, F. O. (1940) *New Engl. J. Med.*, **222**, 174

Treatment

Sulphanilamide in Post-operative Peritonitis

D. C. Cory *et al.*, in a series of 273 cases of appendicitis, treated 252 by appendicectomy and there were no deaths. Twenty-six of them had general peritonitis and were treated with sulphonamide preparations. Three patients in this group died. Fifteen others had appendix abscesses and also were treated with sulphonamide preparations. There were no deaths in this group. For the whole series of 273 cases this represents the low mortality of 1.1 per cent. Soluseptasine, proseptasine, and sulphanilamide were used. Soluseptasine was given in doses of 0.5 g. either intramuscularly or intravenously 4-hourly for 3 doses, then 0.5 g. 6-hourly either as above, or by rectum or mouth. As soon as the patient was doing well clinically the soluseptasine was changed to proseptasine 1 g. three times daily by mouth until the temperature had been normal for 24 hours.

Sulphanilamide was given at first intramuscularly in the form of a 5 per cent solution, later by rectum, and afterwards orally, a total of 6.5 g. being given in the first 24 hours. Some of the cases showed toxic symptoms, and then the drug was stopped. Toxic symptoms were not so common with soluseptasine and proseptasine treatment. In many of the cases anaerobic and actinomycotic organisms were isolated from the peritoneal cavity and the sulphanilamide was found to be active against them.

Healing of Appendical Stump

T. Kross experimented with rabbits to find the best method of dealing with the stump of the appendix after appendicectomy. If it is buried, the stump is converted into a necrotic mass and haemorrhages occur under the mucosa in the adjacent caecal wall. Healing is accompanied by extensive adhesion between the stump and the neighbouring tissue, haemorrhagic infarction in the caecum between the ligature and purse-string suture, and ulceration of the mucosa in this situation. Lymphadenitis occurs and pericaecal abscesses sometimes form. When the stump is merely ligated, the tissue proximal to the ligature is unaffected, fewer adhesions form during healing, and the necrosed stump is separated from surrounding structures by a well-marked zone of fibrous connective tissue. Kross therefore concluded that simple ligature was the safest method of treating the appendical stump.

Drainage after Appendicectomy

R. B. Miles compares the results of drainage and non-drainage in 2 series of appendicectomies. In the 'drainage period', 1925-1930, there were 464 appendicectomies in 55 per cent of which, exclusive of those with an appendix abscess, drainage was adopted with a mortality of 12 per cent. In the 'non-drainage' series, 1934-1938,

there were 726 appendicectomies of which drainage was employed in 4.5 per cent, excluding those with abscess. The mortality in the undrained cases was a half to a third that in the 'drainage period', and the incidence of intra-abdominal complications requiring further operation in the 1934-1938 series was only 2.5 per cent of that in the 1925-1930 series.

Peritonitis

Sulphanilamide. J. S. Raydin *et al.* reported 809 cases of appendicitis with complications. The last 257 of them were treated with sulphanilamide. In the first 552 cases the mortality-rate was 1.4 per cent, whereas in the sulphanilamide-treated group it was only 0.4 per cent. The greatest number of cases in this series occurred at from 20 to 30 years of age. Peritonitis was seen in 355 of the patients. The organisms most commonly found in the peritoneal cavity were *Escherichia coli* and less often streptococci, haemolytic and non-haemolytic. Appendectomy was performed as soon as possible in all cases. Spinal anaesthesia was the anaesthetic of choice in those over 15 years of age. A McBurney incision was used and drainage instituted whenever there was fibroplastic exudate on surfaces other than the appendix, when gross faecal contamination occurred, and in the presence of frank pus. Post-operative treatment consisted in rest for the patient and the viscera. Nothing was given by mouth or rectum for the first few days, fluids being given intravenously. In the second group of patients sulphanilamide was given to all those who had been drained, and to occasional border-line cases. In patients with spreading peritonitis it was given intravenously as an 0.8 per cent solution in physiological saline. The dose was usually 8 g. on the first day, reduced by 1 g. each day. In those with milder infections the initial dose was 6 g. Each daily dose was divided into 6 and given at 4-hourly intervals. Complete blood counts should be made every 24 to 48 hours to detect the development of anaemia or leucopenia. The authors concluded that sulphanilamide is a good drug in the treatment of peritonitis. Since cases responded no matter what the causative organisms it was thought that it is the nature of the lesion, rather than any specific infection, that makes it respond to sulphanilamide.

Appendectomy in Old Age

H. Gardiner reports successful appendicectomy in a woman, aged 84, with a perforated gangrenous appendix and general peritonitis. Within a year there had been two slight attacks and one rather more severe attack when operation was not advised because of her age. It was noteworthy that the patient was fearless of the operation and mentally calm and confident throughout the illness.

Corry, D. C., Brewer, A. C., and Nicol, C. (1939) *Brit. med. J.*, **2**, 561.

Gardiner, H. (1940) *Brit. med. J.*, **1**, 436.

Kross, I. (1939) *Arch. Surg., Chicago*, **39**, 1016.

Miles, R. B. (1939) *Brooklyn Hosp. J.*, **1**, 133.

Raydin, J. S., Rhoads, J. E., and Lockwood, J. S. (1940) *Ann. Surg.*, **111**, 53.

ARRHYTHMIA

See also B. I. M. P., Vol. II, p. 10, and Surveys and Abstracts 1939, pp. 59 and 223.

Tachycardia and Bradycardia

Diagnosis

The sign of the unbalanced pendulum. P. Isaac-Georges reported on a sign, elicited by auscultation, in patients with cardiac failure, and with either tachycardia or bradycardia. This sign, called the sign of the unbalanced pendulum, was characterized by the exaggeration of the normal inequality of the two cardiac 'silences'. This is exactly contrary to the views held by most teachers.

Isaac-Georges, P. (1939) *Monde med.*, **49**, 701.

Heart-Block

Treatment

Digitalis. -H. L. Blumgart and M. D. Altschule considered the question of giving

digitalis to those suffering from partial heart-block, and concluded that it was not contra-indicated in this condition. They studied 19 patients, aged 15 to 72, suffering from congestive heart failure. Heart-block was due to coronary sclerosis in 14 and rheumatic heart disease in 5 of them. Powdered digitalis leaf (0.1 g = 1 cat unit) was given according to body weight, digitalization being accomplished in 3 to 9 days. The dose varied from 1 to 2.3 g. per 100 pounds body weight and averaged 1.3 g. Six patients developed nausea, but there was no change in their P-R interval. There was no change in the P-R interval of 11 of the 19 cases. In 6 cases it was slightly lengthened and in 2 shortened by 0.04 second and 0.08 second. No change in the sequence of auricular ventricular contractions was seen except in one case in which the occasional 2 to 1 heart-block disappeared and a normal 1 to 1 response resulted. The patients improved clinically and the dose was therefore considered adequate. It was stressed that a large dose of digitalis, although producing no toxic symptoms, may be larger than is necessary to control the heart condition. The authors considered it important to realize that, although no untoward effects were encountered in this series, it is possible that digitalis could produce complete heart-block in such patients, and it is therefore important to watch them carefully when they are receiving the drug.

Blumgart, H. L., and Altschule, M. D. (1939) *Amer. J. med. Sci.*, **198**, 455.

Auricular Fibrillation

Treatment

Digitalis. W. Weinstein *et al.* report their observations on the failure of digitalis, recorded by Blumgart and Boas and others, in some cases of auricular fibrillation. They conclude that this was due either to incomplete digitalization or to the presence of a slow ventricular rate and small pulse-deficit quite independent of digitalis. Inadequate dosage of digitalis and a slow ventricular rate (not due to digitalis) appear to be the two chief factors which prevent the effective action of digitalis during exercise and presumably during emotional upsets. Large doses of digitalis lessen the ventricular acceleration which occurs after a standard exercise test in ambulatory patients with auricular fibrillation, and at the same time decrease the pulse deficit, but are not effective in patients already having a slow ventricular rate. Prolonged rest, as well as large doses, might be required to produce slowing. The tendency to prevent acceleration during exertion and emotional stress is one of the clinical benefits derived from digitalization.

Boas, I. P. (1929) *Amer. Heart J.*, **4**, 499.

Blumgart, H. (1924) *Heart*, **11**, 49.

Lewy, H., and Boas, I. P. (1938) *Amer. Heart J.*, **15**, 643.

Weinstein, W., Plaut, I., and Katz, I. N. (1940) *Amer. J. med. Sci.*, **199**, 498.

Auricular Standstill

I. I. Rosenbaum and S. A. Levine reviewed 8 cases of auricular standstill, a condition in which the auricles cease to beat, while the ventricles continue to beat with an independent, regular rhythm. A study of these cases confirmed the belief that digitalis and quinidine intoxication are the most common causes of auricular standstill. When there is electrocardiographic evidence of its presence the nature and dosages of the drugs being given the patient should be investigated and adjusted. The disorder tends to occur more commonly in older patients who are in congestive failure from serious heart disease. Auricular standstill due to quinidine tends to be more transient than that due to digitalis.

Rosenbaum, I. I., and Levine, S. A. (1939) *Amer. J. med. Sci.*, **198**, 774.

Systolic Gallop Rhythm

Mechanism

C. C. Wolferth and A. Margolis report 2 cases of systolic gallop rhythm in which an attempt was made by means of sound tracings and other methods to confirm the mechanism of production of the second sound. It is shown that there are at least two types of systolic gallop rhythm, exclusive of various other sounds between the first and second heart sounds. In one of the types of systolic gallop rhythm the

additional sound is heard best over the aortic area; this is called aortic systolic gallop rhythm. In the other type the additional sound is heard best over the apex; this is called the apical systolic gallop rhythm. The additional sound in aortic systolic gallop rhythm appears to originate in the aorta; it may be caused by sudden checking of the distension of the aortic wall during systole, or by impact of the aorta against surrounding structures at that instant. Some abnormality of the heart beat or of the aortic wall seems to be necessary for the production of this sound. It has been specially noted in aortic insufficiency, typhoid or typhoid-like fevers, and hypertensive heart disease. The cause of the additional sound in apical systolic gallop rhythm remains obscure; but it may be related to impact of the heart's apex against the chest wall.

Wolferth, C. C., and Margolies, A. (1940) *Amer. Heart J.*, **19**, 129.

Arrhythmia in Hypertensive Heart Disease

N Flaxman reports 243 cases of arrhythmia among 800 cases of hypertensive heart disease, an incidence of 30 per cent. The most common arrhythmia was auricular fibrillation, which was present in 198 cases (81.5 per cent). This condition had the best prognosis in cases in which the fibrillation preceded and precipitated congestive heart failure. Arrhythmia may occur at any time during the course of hypertensive heart disease, and is often the first indication of cardiac involvement. It does not tend to show spontaneous remission, to change in character, or to become associated with, or followed by, another type of arrhythmia. The mortality among patients with arrhythmias was lower than among those with regular sinus rhythm, owing to the comparative absence of coronary thrombosis. Of patients with auricular fibrillation 75 per cent, of those with auricular flutter, paroxysmal tachycardia or complete heart-block 66 per cent, of those with extrasystoles 65 per cent, and of those with nodal rhythm 50 per cent survived, some for a considerable number of years. Among patients with a regular rate above 100 per minute there was a mortality of 39.2 per cent, whereas among those with a regular normal rate the mortality rate was 20.3 per cent. Of those with sinus tachycardia 80 per cent had combined ventricular (congestive heart) failure, as compared with only 60 per cent of those with a normal sinus-rate and rhythm. Since arrhythmia often led to myocardial insufficiency, treatment with digitalis or quinidine sulphate was necessary.

Flaxman, N. (1940) *Arch. intern. Med.*, **65**, 595.

ARTERIAL DISEASE AND DEGENERATION

See also B.F.M.P., Vol. II, p. 39, and Surveys and Abstracts 1939, pp. 61 and 224.

Periarteritis Nodosa

Clinical Picture

R. Fitz *et al.* record periarteritis nodosa in a woman under observation for 26 months. Symptoms were first noticed at the age of 26 years, 11 years before death. Clinically it began with subjective quivering and stiffness of the facial muscles, and 3 years later the same sensations occurred in the legs which, another 3 years later, were easily fatigued, swelled after use, and showed red spots when she stood too long. She had occasional diarrhoea, an irritating chronic cough, and a few seconds' delay in accommodation. About this time she came under medical care, and then showed fixed irregular pupils, a tongue deviating to the left, exaggerated arm jerks, absence of abdominal reflexes and knee- and ankle-jerks, poor position and vibration sense in the legs, positive Rombergism, and stocking hyperaesthesia in the legs. The first diagnosis was disseminated sclerosis; later, a beefy red tongue and diarrhoea suggested non-tropical sprue. Bouts of fever began, followed by cutaneous lesions—wheals, erythema, papules, and purpuric spots. The disease then progressed with short incomplete remissions. A gall-bladder full of stones was removed, and multiple haemorrhages were then noticed on the stomach and duodenum. Some time

later, periarteritis nodosa was suggested, and re-examination of the gall-bladder sections showed typical lesions. Necropsy showed lesions in all stages of development. In the progress of the disease the heart had enlarged without congestive failure. The clinical renal findings were those of a varying and transitory acute nephritis with progressive hypertension.

Abdominal symptoms—P. D. Allen also records the case of a man who had recently recovered from gonorrhoea and 6 weeks before admission to hospital was attacked by pain in the back. On admission he appeared to be 'chronically and acutely' ill with fever and a leucocytosis of 18,000. Various diagnoses—right perinephric abscess, appendix abscess, cholecystitis, and, lastly, perforated peptic ulcer—were offered. Laparotomy showed that the appendix was normal to the naked eye, but it and the chronically inflamed gall-bladder were removed. But histologically the gall-bladder, and at a subsequent necropsy other parts of the body, showed periarteritis nodosa. The author prefers the name polyarteritis nodosa, and mentions that the medium-sized and smaller arteries are predominantly affected and the renal arteries almost always involved. Reference is made to Singer's account of 2 cases with acute abdominal symptoms.

Allen, P. D. (1940) *Arch. Surg., Chicago*, **40**, 271.

Fitz, R., Parks, H., and Branch, C. F. (1939) *Arch. intern. Med.*, **64**, 1133.

Singer, H. (1927) *Arch. intern. Med.*, **39**, 865.

Thrombo-angiitis Obliterans (Buerger's Disease)

Treatment

Sodium tetrathionate and sodium thiosulphate—F. V. Theis and M. R. Freeland stated that thrombo-angiitis obliterans is associated with changes in the blood and tissue metabolism, as well as peripheral arterial and venous thromboses and local infection of the involved extremity. The blood changes include increased viscosity, rapid sedimentation and coagulation, increased alkalinity, and arterial-like oxygen saturation of the superficial venous blood from the involved extremity. Smoking, a probable aetiological factor, has been shown to lower the peripheral temperature and decrease both the arterial and venous oxygen saturation in patients with the acute disease. The authors have had considerable clinical success in treating the condition with sodium tetrathionate in doses of 0.6 g., and sodium thiosulphate in doses of 2 g. daily. These substances, injected intravenously, produced the opposite effect from smoking. The thiosulphate produced a rapid rise in skin temperature, whereas the tetrathionate produced a slower, more prolonged rise. The oxygen saturation of both arterial and venous bloods was also substantially increased by these drugs. This increased oxygen saturation is not associated with an increase in total haemoglobin or red-cell count. It seems probable that an inactive form of oxyhaemoglobin is present on which the sulphur compounds act as catalysts. The actual catalyst formed may be glutathione, which contains sulphur. The injection of these drugs increases both the liver and blood glutathione.

The oscillating bed—N. W. Barker treated 88 cases of occlusive arterial disease of the legs on a bed attached to a special cradle, so that it can be rocked by means of an electric motor in a transverse axis, through an arc of approximately 60 degrees, at a slow regular rate. The period of oscillation can be adjusted to take from one to seven minutes for a complete cycle. The oscillations should be adjusted so that the feet show blanching when elevated and rubor when dependent for a few seconds only. The cases included thrombo-angiitis obliterans, arteriosclerosis obliterans, and embolic arterial occlusion. The treatment was found not to influence the pain of intermittent claudication. Given without other forms of therapy, this treatment, however, favourably influenced prethoracic pain, pain of ischaemic neuritis, and that of gangrene and ulceration in 33 per cent of the cases treated. The treatment can be given intermittently or continuously and combined with other local and general measures.

Barker, N. W. (1939) *Proc. Mayo Clin.*, **14**, 618.

Theis, F. V., and Freeland, M. R. (1940) *Arch. Surg., Chicago*, **40**, 190.

Occlusion of Brachial Artery

Causing Volkmann's Ischaemic Contracture

L. W. Plewes described a case of occlusion of the brachial artery which led to Volkmann's ischaemic contracture. The patient, a child of 7 years, fell from a tree and sustained a compound fracture of the arm including injury to the brachial artery and the median nerve. When admitted to hospital she had no radial pulse on that side and the hand was blue and cold. Operation was performed and all damaged tissue was removed. The fracture was reduced and a piece of brachial artery containing a thrombus was resected. About 5 minutes later the hand became warm. The arm was then put in a collar-and-cuff sling, but in spite of such prompt treatment ischaemic contracture eventually occurred. Trophic changes appeared in the parts supplied by the median nerve.

Plewes, L. W. (1940) *Brit. med. J.*, **1**, 1054.

Thrombosis of Abdominal Aorta

H. C. Lueth reports 4 cases of thrombosis of the abdominal aorta, which illustrate the variability of the clinical picture. In one case the thrombosis was secondary to rheumatic carditis, and the patient had sharp, cramp-like pain in the upper abdomen; this disappeared slowly within 3 days. Some months later there was a further attack, with an irregular pulse of 115 to 120, hepatic enlargement, severe and colicky pain, localized to the umbilicus, this region soon becoming tender and rigid. The blood-pressure fell to 85/60 mm. Hg, and the patient grew progressively worse, comatose, and died on the fourth day. A second case followed detachment of a mural thrombus from an aneurysm of the abdominal aorta. Initial dull pain in the epigastrium was followed next day by a sudden severe pain in the left upper quadrant. There was tenderness in the upper abdomen, and a pulsatile mass, the size of a grapefruit, was palpable in the left hypochondrium. Nausea, vomiting, and rigidity followed and the patient died in 18 hours.

Lueth, H. C. (1940) *Ann. intern. Med.*, **13**, 1167.

Pseudo-Thrombotic Occlusion of Femoral Artery

F. S. Stafford describes a rare arterial lesion for which the name 'pseudo-thrombotic occlusion' is suggested. A man, aged 48, was admitted to hospital for cramp in the muscles of the left leg, brought on by walking several hundred yards; this disappeared after a few minutes' rest, but reappeared when he walked again. He appeared to be in excellent general condition, there was no evidence of arteriosclerosis, and the blood-pressure was 122/78 mm. Hg. The left leg was slightly atrophic, and pulsation could not be felt below the left inguinal (Poupart's) ligament. A faint systolic bruit was heard over the left femoral artery just below the inguinal ligament. The results of clinical and blood examinations were negative, the urine was normal, the electrocardiogram did not show any evidence of cardiac disease, and radiologically there was no sign of arterial calcification. Under spinal anaesthesia the left common femoral artery was exposed, and the first portion of the common femoral artery was found to be enlarged for a distance of 3 cm.; this enlargement felt rubbery and solid, and did not pulsate. Below the enlargement the artery appeared and felt normal, but did not pulsate. The artery was isolated and clamped above and below the enlarged portion, and was then incised longitudinally. As soon as the muscular coat was divided a quantity of light yellow gelatinous material oozed forth. When this had been evacuated the intima of the artery was seen to be intact, the gelatinous material evidently having been enclosed within the vessel wall outside the intima. The cavity was irrigated with physiological saline and the outer wall of the artery was then closed with a continuous silk suture. On removing the clamps, pulsation was now returned throughout the length of the artery, and after operation the left foot was warm with strong pulsations in the dorsalis pedis and posterior tibial arteries. Recovery was uneventful. Microscopical examination of the gelatinous material indicated that it was coagulated plasma which contained neither cellular elements nor blood pigment. The aetiology of this curious condition is obscure.

Stafford, E. S. (1940) *Johns Hopk. Hosp. Bull.*, **66**, 253.

Chronic Arteritis*Pathology*

Changes in elasticity of aorta with age.—J. Krafka investigated the changes in the elasticity of the aorta with age. Some workers consider that the change in elasticity is not progressive, but that there is an increase in distensibility from birth to the twentieth year, with a gradual decline from that time to old age. The author's investigations showed that there is not any increase in distensibility from birth up to the twentieth year, but that there is a gradual loss in elasticity with age throughout life. Loss in elasticity of the aorta with age is ascribed to 2 factors. (a) distensibility, 80 per cent, and (b) fibrosis, 20 per cent. No direct correlation exists between elasticity, blood-pressure, sclerosis, and thickness of the aortic wall.

Krafka, J., Jnr (1940) *Arch. Path.*, **29**, 303.

Peripheral Circulatory Disturbances Generally*Treatment*

Prostigmin. S. Perlow employed prostigmin in 31 cases of peripheral circulatory disturbance, including 11 of thrombo-angitis obliterans, 4 of arteriosclerosis, 9 of Raynaud's disease, 5 of acrocyanosis, and 2 of acute vascular occlusions. At first each patient was given a subcutaneous injection of 0.5 mg. of the drug, the temperature of the affected extremity being noted to determine the degree of vasodilatation produced. The patients were then given 7.5 mg. 3 times daily by mouth, at 6-hourly intervals for a week, without any other treatment. If no improvement occurred, the dose was increased to 15 mg. Of the 11 cases of thrombo-angitis obliterans there was an improvement in the walking distance and an elevation of the digital skin temperature in 7, and no improvement in 4. In only one of the 4 cases of arteriosclerosis did improvement occur. Of the 9 cases of Raynaud's disease there was marked improvement, i.e. complete disappearance of attacks of vasospasm, in 5 cases with mild attacks, and slight improvement in one case with moderately severe attacks. There was no improvement in 3 severe cases. Of the 5 cases of acrocyanosis, there was marked improvement with return of colour of the hands to normal in one case. In the 2 cases of arterial occlusion, the drug was given subcutaneously, there was rapid and marked improvement in the condition of the skin, which became warm and normal. Most of the cases were able to tolerate doses of from 45 to 60 mg. of the drug orally, without having abdominal cramps.

Perlow, S. (1940) *J. Amer. med. Ass.*, **114**, 1991.

Peripheral Vascular Diseases Generally*Treatment*

Passive vascular exercises.—A. Silverglade confirmed experimentally the work of Landis and Gibbon on the production of vasodilatation in the lower extremities in response to immersion of the forearms in warm water. The reported vasodilator effect of ethyl alcohol does not as a rule occur in the lower extremities which have been allowed to cool spontaneously in a constant temperature room at 71° to 73° F. Upon examination of 246 patients, 60 (24 per cent) were found unsuitable for passive vascular exercise treatments. These patients did not receive the treatment either because of specific contra-indications or because they did not have peripheral arterial deficiency. Accurate diagnosis of the cause of symptoms in the extremities must always be made before suction-pressure therapy is advised, so that patients may not be disappointed and a useful treatment fall into disrepute. Of 123 cases of peripheral vascular disease that had received the minimum of 24 hours of treatment, 76.4 per cent were improved.

Silverglade, A. (1940) *Arch. phys. Ther.*, **21**, 100.

Cigarette Smoking and Deep Breathing*Effects on Peripheral Vascular System*

M. G. Mulinos and I. Shulman investigated the effects of cigarette smoking and deep breathing on the peripheral vascular system. They concluded that deep

breathing alone could account for most of the decreased blood inflow rate, the loss of hand volume, and the drop in skin temperature of the hand resulting from the inhalation of cigarette smoke. Those who did not inhale cigarette smoke showed a greater vascular response of the hand from 10 deep breaths than from the puffing, and a lesser response than those who inhaled the smoke. Inhaling the smoke from de-nicotinized cigarettes resulted in as great, and occasionally greater, vasoconstriction than inhaling the smoke from an ordinary cigarette. The vasoconstriction due to smoking lasts 15 minutes.

Mulinos, M. G., and Shulman, I. (1940) *Amer. J. med. Sci.*, **199**, 708

ARTHRITIS

See also B.F.M.P., Vol. II, p. 65, Cumulative Supplement, Key Nos. 94-102, and Surveys and Abstracts 1939, pp. 135 and 226

Acute Suppurative Arthritis

Treatment

Sulphanilamide.—W. W. Spink treated a man, aged 35 years, suffering from acute *beta*-haemolytic streptococcal sepsis, with sulphanilamide. The illness began with tonsillitis and the patient then developed pneumonia, acute glomerular nephritis with uraemia, and suppurative arthritis of a knee joint. Three days after admission to hospital he was given 40 grains of sulphanilamide a day for 3 days. This was then increased to 60 grains a day and after a week's treatment his temperature became normal. During the second week of treatment he developed diarrhoea, which may have been due to his uraemia. The drug was stopped for a few days and then continued until aspiration of the synovial cavity of the knee joint yielded a sterile fluid on two occasions. This was 3 weeks after the beginning of treatment and 2 weeks later the patient had completely recovered with full extension and almost full flexion of the knee joint. When joint lesions of this type are treated by surgical drainage, ankylosis usually results. Examination of the synovial fluid before treatment showed the organisms to be mostly extracellular; after treatment they became mainly intracellular, any extracellular ones being pleomorphic. During treatment the level of free sulphanilamide in the synovial fluid approximated to that in the blood.

Spink, W. W. (1939) *Amer. J. med. Sci.*, **198**, 35

Gonococcal Arthritis

Treatment

Sulphanilamide.—O. S. Culp and M. C. Cobey describe the treatment by sulphanilamide of 50 cases of gonococcal arthritis of whom 82 per cent were either cured or greatly improved. The best results were noted in the acute cases, among which there were no complete failures, and 75 per cent were discharged well, and an additional 14 per cent markedly improved. In the subacute group 5 out of 10 patients were cured and 3 showed well-marked improvement. Four chronic cases responded poorly to the drug. The period of treatment varied from 3 to 33 days, with an average of 11 days. The total amount of the drug in the cured cases averaged 54.3 g., or approximately 4.5 g. daily. Sulphanilamide therapy should be begun as soon as possible. The acutely infected joints should be immobilized to relieve acute symptoms. The patient should be given 1.2 g. of the drug with an equal quantity of sodium bicarbonate, 4-hourly, until a blood-level of at least 8 mg. per 100 c.cm. has been reached. When this level is reached, the dose should be halved and then, if the blood-level still continues to rise, the dose should be reduced to 0.3 g. every 4 hours. In most cases the drug is discontinued 4 days after the complete disappearance of the joint manifestations.

Culp, O. S., and Cobey, M. C. (1940) *J. Bone Jt Surg.*, **22**, 185.

Rheumatoid Arthritis

Aetiology

Sulphur metabolism — R. H. Freyberg *et al.* in a carefully controlled investigation, found that there was not any evidence of sulphur deficiency or of any abnormality in sulphur metabolism in patients with rheumatoid arthritis. No biochemical or metabolic indication of need for, or benefit from, sulphur medication in the treatment of rheumatoid arthritis was found.

Treatment

Gold therapy — D. Sashin *et al.* reviewed the literature of the treatment of rheumatoid arthritis with gold salts and reported the results obtained in 80 patients. Of these 43.75 per cent were markedly improved and 38.75 per cent moderately so. In 17.5 per cent there was no improvement. Of 11 patients with ankylosing spondylitis 54.55 per cent were improved. 19 of the cases developed toxic reactions such as pruritus, urticaria, and stomatitis and in 3 of them the treatment had to be stopped. The treatment should only be given for rheumatoid arthritis, and has many contraindications such as asthma, pregnancy, and anaemia. Although gold therapy is valuable in the treatment of rheumatoid arthritis it must be used with caution owing to the toxic reactions it produces.

Colloidal sulphur — N. R. Abrams and W. Bauer investigated the effects obtained from the administration of sulphur in 14 patients with rheumatoid arthritis, 12 of whom were ambulatory and 2 hospitalized. A course of colloidal sulphur was administered intravenously to 10 patients, and intramuscularly to 2, the remaining 2 patients each received 2 intravenous courses. The initial dose was 20 mg., followed by doses of 30 mg. in 12 of the cases. Two cases received 30 mg. initially, followed by one dose of 50 mg., and subsequent doses of 100 mg. Ten patients received a total dose of 310 to 370 mg. of colloidal sulphur during 6 to 8 weeks, four received a total of 640, 1080, 1200 and 2900 mg. respectively. Subjective improvement, consisting of increased strength and less joint pain, was noted after 8 of the 16 courses of treatment in the 14 patients. No patients improved objectively. The authors conclude that colloidal sulphur, even in large doses, does not alter the course of rheumatoid arthritis, as measured by objective or laboratory evidence of improvement in well-controlled cases.

Histamine — R. O. Muether stated that the subcutaneous injection of histamine diphosphate solution, 1 in 1,000, increases mobility and often relieves pain in patients with rheumatoid arthritis without complete ankylosis of the joints. Injection of the drug appears to be as satisfactory as iontophoresis, and much superior to inunction. It does not cure arthritis but is a good adjunct to the use of other methods of treatment. To avoid severe reactions the drug should be given cautiously. It appears to have no cumulative or deleterious effects. It apparently enhances the value of other forms of therapy, and in many cases enables the patient to carry on activities which would otherwise be impossible. A test dose of 0.1 c.cm. should be given, and increased by 0.1 c.cm. until a reaction level is reached. This reaction-producing dose is then maintained until the patient's tolerance increases. In the author's experience 0.4 to 0.6 c.cm. is the range of effective dosage, and may be carried on for 3 to 6 months before tolerance is increased. Reactions consist of headaches, flushing, palpitation, sweating, nausea, dizziness, and weakness.

Vitamin C — M. G. Hall *et al.* found that in a group of 56 cases of rheumatoid arthritis 75 per cent had a subnormal content of vitamin C in the blood, 59 per cent had levels below 0.5 mg. per 100 c.cm. Although some of the patients had had diets containing vitamin C well below the amount usually required for normal people, none of them presented clinical evidence of scurvy. Patients with rheumatoid arthritis have a much greater demand for vitamin C than the normal individual. It was shown, in 10 people with rheumatoid arthritis, that they could tolerate an intake of over a 100 mg. of vitamin C and usually 200 mg. without marked excretion in the urine. All patients with rheumatoid arthritis in the authors' hospital were given 200 mg. of vitamin C per day for 8 months, without, however, showing any improvement that could be attributed to the effect of the vitamin.

Bee venom — I. C. Hill publishes some practical observations on the various methods of treatment, especially on the scope and limitations of physiotherapy.

Physiotherapy—the whole range of balneotherapy, electrotherapy, and massage—alone is disappointing in rheumatoid arthritis, though not in fibrositis; it has an important place as a part, but not the whole, of the treatment of rheumatoid arthritis. Unless visits to the bath are restricted (and this often requires powerful persuasion in the face of the inclusive all-in tariffs so popular with spa authorities) and are liberally interspersed with adequate periods of rest, a state of 'thermal debility' will result. Some years ago, in collaboration with J. Barnes Burt, the author treated 50 patients with rheumatoid arthritis by intradermal injections every 3 or 4 days of bee venom, at first apicozan and later a more effective preparation, obtained privately; the usual course of baths and massage was given and the results compared with those of 50 controls receiving baths and massage only. The following conclusions were reached: bee venom is not a specific cure for rheumatoid arthritis; it has not any bad results; the general condition of patients receiving bee venom and physiotherapy was better than that of the controls; the bee venom was valuable in fibrositis, panniculitis, and neuritis. Cold treatment has more value than any other single method of treatment. Psychotherapy, consciously or unconsciously applied, is an essential in the successful treatment of those difficult patients who are prone to respond unduly to any suggestion, particularly an unhealthy one. Thus any hesitation or loose talk by the practitioner about general debility, anaemia, or low blood-pressure will be accepted and exploited with increase in the symptoms, especially of lonely middle-aged spinsters with unhappy surroundings.

Artificial fever—W. M. Solomon and R. M. Stecher stated that, in their experience, artificial fever therapy failed to cure a single case of rheumatoid arthritis, or even failed permanently to arrest the disease. It, however, gave partial relief of pain and stiffness in 85 out of 114 patients (75 per cent). At times relief persisted for only one or two days, but occasionally it continued for several weeks. In some cases 3 or 4 treatments a year were sufficient to keep patients relatively comfortable and active.

Splenectomy—F. Bach and O. Savage report 3 cases in which splenectomy was performed for rheumatoid arthritis. In two cases well-marked clinical improvement followed, and in the remaining patient, although there was not this improvement, the disease was stated to be arrested; in all the cases these results occurred 9 months after the operation. In 2 cases there was amyloid disease. Previously recorded cases of operation were noted, by Hanrahan and Miller, by Loeper, Lemiere and Patel (in Still's disease), and others.

- Abrams, N. R., and Bauer, W. (1940) *New Engl. J. Med.*, **222**, 541.
 Bach, F., and Savage, O. (1940) *Ann. Rheumat. Dis., Lond.*, **2**, 47.
 Lieberg, R. H., Block, W. D., and Fromer, M. I. (1939) *J. Amer. med. Ass.*, **113**, 1063.
 Hall, M. G., Darling, R. C., and Taylor, I. H. I. (1939) *Ann. intern. Med.*, **13**, 415.
 Hanrahan, I. M., and Miller, S. R. (1932) *J. Amer. med. Ass.*, **99**, 1247.
 Hill, L. C. (1940) *Brit. J. Rheumatism*, **2**, 202.
 Loeper, M., Lemiere, A., and Patel, J. (1937) *Pr. méd., Paris*, **45**, 625.
 Muehrer, R. O. (1940) *Ann. intern. Med.*, **13**, 2147.
 Sashin, D., Spanbock, J., and Kling, D. H. (1939) *J. Bone Jt. Surg.*, **21**, 723.
 Solomon, W. M., and Stecher, R. M. (1940) *Arch. phys. Ther.*, **21**, 339.

Menopausal Arthritis

F. C. Hall reports that from examination of 71 female castrates who began to show joint symptoms a few weeks after castration, 53 were more accurately called arthralgia because there was not any evidence of structural change. Like other menopausal symptoms, the arthralgia can, in the absence of infection, excessive fatigue, trauma and extreme emotional disturbance, be controlled by 10,000 to 20,000 iat units of oestrogenic substance a week for 6 weeks, of the 40 of the 53 cases in which adequate treatment was given, 70 per cent were almost completely relieved of joint and muscular pain. In the 18 patients with arthritis as well as arthralgia, treatment with oestrin controlled flushes, sweats, and arthralgia, and in several instances the arthritis. Arthralgia and arthritis would appear to be phases

of the same process due to excess of anterior pituitary hormone in the absence of ovarian hormone. P. S. Hench considered that several different conditions were included under the term menopausal arthritis by those who used the name, and that the morbid changes had not been settled. His experience with theelin (oestrone) was disappointing and he did not consider that such treatment should be advocated. R. L. Cecil also had been disappointed by treatment by ovarian hormones and now relied more on physical measures, diet, and reduction in weight than on endocrine treatment.

Cecil, R. L. (1939) *J. Amer. med. Ass.*, **113**, 1062.

Hall, F. C. (1939) *J. Amer. med. Ass.*, **113**, 1061.

Hench, P. S. (1939) *J. Amer. med. Ass.*, **113**, 1062.

Spondylitis Deformans

Treatment

Endocrine therapy.—A. H. Lemmery and O. Koddermann employed endocrine therapy in 45 cases of spondylitis deformans. Testosterone propionate, 5 mg., and anterior pituitary extract, 100 mouse units, were given alternately to 28 cases, and endocrine and X-ray therapy to another 17 cases. Judged by criteria of improved chest breathing, sedimentation rate, and general physical mobility, 22 of the 28 cases showed considerable expansion in thoracic breathing. The authors held the view that the condition is a vertebral disease of an inflammatory nature in which endocrine dysfunction is present, but the evolution of which is governed by a focal toxicosis which can be demonstrated clinically and serologically in every case.

Lemmery, A. H., and Koddermann, O. (1939) *Med. Welt*, **13**, 1621.

Aspiration of Joint Effusions

D. H. Kling strongly advocates aspiration of joints for both diagnosis and treatment, and in several thousand aspirations performed in all forms of joint disease, including septic and tuberculous cases, has never seen any bad effects. He aspirates joints if they do not respond to other forms of treatment in a week. Aspiration is specially effective in acute infections with highly turbid fluid when combined with lavage of the joint. In rheumatoid arthritis and osteoarthritis benefit is temporary only, but it is nevertheless of therapeutic value as it increases the efficacy of other measures.

Kling, D. H. (1939) *The Synovial Membrane and the Synovial Fluid*, London, p. 227.

Treatment of Different Types

Vitamin C and Sanocrysin

K. Secher stated that many of the reactions with sanocrysin (gold and sodium thiosulphate) therapy are similar to those due to vitamin deficiency. He had previously pointed out the importance of employing large doses of vitamins A, B, and C in conjunction with sanocrysin treatment. This treatment was particularly effective in thrombopenia and dermatitis. Pemberton (1935) showed that abnormal blood-sugar curves are found in arthritis and indicate a decreased tolerance of sugar. Secher showed that this was associated with the absence from the blood of ascorbic acid and that if the quantity of ascorbic acid is increased to normal, the curve becomes normal. The author considered that the importance of the administration of vitamins during treatment with sanocrysin was confirmed as regards thrombopenia and skin reactions, in which ascorbic acid acts beneficially. Decreased tolerance of carbohydrates can be abolished in many infectious diseases by increasing the amount of ascorbic acid in the blood.

Colloidal Iodized Sulphur

The role of sulphur in the nutrition of bones and the fact that sulphur metabolism is disturbed in osteoarthritis, led I. I. Lubowe to treat the condition with colloidal iodized sulphur. Two capsules (each containing 10 mg. of colloidal sulphur and 5 mg. of colloidal iodide, 50 per cent of which consists of iodine, in 2½ minims of olive oil) were given after meals for a few days, then 1 capsule after meals for 30

days. Vitamins, salicylates, and iron might also be indicated by the symptoms and might be given in conjunction with the capsules. Of 10 patients with rheumatoid or osteoarthritis, 8 were benefited by this treatment, gaining in weight and appetite, and showing decreased fatigue. In 2 cases there was no response to the treatment. There were no adverse reactions to the drug in this series.

Oestrogenic Therapy

A. Cohen *et al.* employed oestrogenic therapy in 23 cases of arthritis, 17 being of the atrophic and 6 of the mixed type. Individual dosages ranged from 10,000 to 100,000 I.U., the initial treatment being generally 10,000 I.U. daily by intramuscular injection and the intervals between dosage being increased to once weekly when improvement was noted. If no improvement occurred the dose was gradually increased to 100,000 I.U. and if, after 3 or 4 such doses, no change was noted, treatment was discontinued. The duration of treatment ranged from 1 week to 3 months. Of the 23 cases, 7 of the atrophic and 5 of the mixed type showed a distinct improvement in joint symptoms. Three patients of the atrophic type showed some improvement and then relapsed, whereas in 7 patients no improvement, either general or local, was observed. The authors concluded that, in menopausal hypertrophic arthritis, the benefits obtained by oestrogenic therapy, though striking, are of a general systemic nature. The joint condition itself must be treated by mechanical readjustments and weight reduction. Little benefit appears to be obtained in women suffering from atrophic arthritis but with no disturbances in menstrual function. Menopausal atrophic arthritis was benefited in a sufficiently large percentage of cases to suggest that this type of therapy has a definite place in the treatment of such cases.

Autohaemotherapy and Artificial Fever

W. K. Ishmael stated that autohaemotherapy combined with artificial fever is of definite value in the treatment of the following types of rheumatic disease: acute fibrositis, chronic fibrositis, acute gonococcal arthritis, juvenile rheumatoid arthritis (Still's disease), acute infective arthritis, and the premenstrual rheumatic exacerbation syndrome. It also increases the effect of oestrogen employed in the treatment of menopausal arthralgia. It is of little, or no, consistent benefit in chronic infective (rheumatoid) arthritis in adults. The technique consists in the resection, before clotting occurs, into the hip muscles of 10 c.cm. of blood withdrawn from the patient's vein. This is immediately followed by one hour of artificial fever therapy at 101° F. This procedure is repeated twice weekly for 8 to 10 treatments, after a rest period of 2 to 4 weeks the course is repeated as indicated.

Cohen, A., Dubbs, A. W., and Myers, A. (1940) *New Engl. J. Med.*, **222**, 140.

Ishmael, W. K. (1940) *Arch. phys. Ther.*, **21**, 335.

Lubow, I. I. (1940) *Chin. Med. Surg.*, **47**, 210.

Secher, K. (1940) *Lancet*, **1**, 735.

Chronic Arthritis

Diagnosis

Serum phosphatase—C. L. Steinberg and L. C. Suter consider that phosphatase plays a large part in calcium metabolism and its deposition in bone. Some authorities have found a high value of serum phosphatase in certain bone diseases, such as chronic arthritis, and a normal value in others. However, in 44 cases of atrophic arthritis, 8 of hypertrophic arthritis, 5 with mixed atrophic and hypertrophic arthritis, and 5 with osteitis deformans, the only case of arthritis with a raised serum phosphatase had malignant disease of the prostate. It had formerly been shown that this increase occurs in this type of malignant disease. Six normal persons were investigated as controls. It was concluded that a rise in serum phosphatase in a suspected case of atrophic or hypertrophic arthritis indicates a wrong diagnosis or the presence of some complication.

Steinberg, C. L., and Suter, L. C. (1939) *Arch. intern. Med.*, **64**, 483.

ARTIFICIAL FEVER THERAPY

Complications*Herpes*

S. I. Warren *et al* found that when 411 afebrile patients were treated with artificial pyrexia herpes simplex developed in 46.2 per cent. The diseases treated included acute or chronic gonorrhoea, chronic rheumatoid arthritis, syphilis of the nervous system, disseminated sclerosis, and neoplasms. Pyrexia was induced by diathermy, radiothermy, infra-red irradiation, and hot baths. The herpes recurred in only 5 per cent, suggesting the development of some immunity following the first attack. In some cases in which the herpes was severe, symptoms took the form of an encephalitis which resolved without sequelae. Some of the strains of virus were found by cross-protection tests on rabbits to be immunologically related to the Frank strain of herpes virus.

Nausea and Vomiting

Treatment by intravenous hypertonic saline. I. F. Rosenberg and N. N. Epstein advocated the intravenous administration of 500 ccm of hypertonic saline solution, 5 per cent, immediately preceding artificial fever therapy. This procedure reduces the incidence, frequency, and severity of nausea and vomiting which frequently occur during hyperpyrexia. It also reduces the incidence and severity of reactions of intolerance to heat and post-therapeutic debility. There are few untoward reactions, and little or no discomfort from this method.

Rosenberg, I. F., and Epstein, N. N. (1940) *Amer. J. med. Sci.*, **199**, 650.

Warren, S. I., Carpenter, C. M., and Boak, R. A. (1940) *J. exp. Med.* **71**, 155.

ASTHENOPIA

Treatment*Vitamin A*

F. C. Cordes and D. O. Harrington report that in 82 cases of persistent asthenopia the aetiological factor was a deficiency of vitamin A. Of this number only 22 per cent gave a history of any degree of night-blindness, but in 31 per cent there was a dietary deficiency often resulting in gastro-intestinal disease. The use of carotene in oil in an average dosage of 10,000 units, three times a day for one month resulted in complete relief in 80 per cent of cases, and partial cure in a further 12 per cent. It was found necessary to continue the carotene in small doses after the initial treatment. The authors are of opinion that cod-liver oil or vitamin A concentrates would be equally effective.

Cordes, F. C., and Harrington, D. O. (1939) *Amer. J. Ophthalm.*, **22**, 1343.

ASTHMA

See also B.F.M.P., Vol. II, p. 179, Cumulative Supplement, Key No. 110, and Surveys and Abstracts 1939, p. 231.

Aetiology*Periarteritis Nodosa and Allergy*

A. Trasoff and M. Scarf report periarteritis nodosa in an asthmatic patient. This confirms the opinion of Cohen, Kline, and Young (1936) that the condition is a manifestation of irreversible allergy in asthmatic and other allergic patients.

Cohen, M. B., Kline, B. S., and Young, A. M. (1936) *J. Amer. med. Ass.*, **107**, 1555.

Trasoff, A., and Scarf, M. (1940) *J. Allergy*, **11**, 277.

Clinical Picture

Periarteritis Nodosa Associated with Asthma

F. M. Rackemann and J. F. Greene, in a preliminary paper, describe what may be a new syndrome, namely asthma, haemic eosinophilia, and periarteritis nodosa, which they observed in 8 cases. On reference to 229 publications 49 more cases were found, thus making 27 in all; in 20, or 74 per cent, there was a high blood eosinophilia. It is pointed out that since 1923, when 70 cases of periarteritis nodosa were on record, an increase in the number of cases of this condition has taken place to about 245, in 15 of which there was eosinophilia without asthma. It was suggested that in 1907 Carnegie Dickson described polyarteritis acuta nodosa as a condition allied to periarteritis nodosa. The authors find that patients with a high haemic eosinophilia are more difficult to treat than other asthmatics, and suggest that this arterial lesion is the final stage of a process which in the beginning is common to many cases of asthma.

Dickson, C. (1907) *J. Path. Bact.* **12**, 50.

Rackemann, F. M., and Greene, J. F. (1939) *Trans. Ass. Amer. Phys.* **54**, 112.

Treatment

Prevention of Attacks

Aminophylline.—B. G. Efron and P. Everett reported their experiences with the use of theophylline with ethylenediamine (aminophylline) in bronchial asthma. The use of the drug was restricted chiefly to the most severe cases, especially those in which adrenaline no longer exerted a definite and lasting effect. Of these adrenaline-fast cases, two-thirds obtained relief which was generally rapid and complete. In a few cases relief was delayed and only partial, and rarely was the drug completely ineffective. Although, even in the most severe attacks of asthma, it was generally unnecessary to administer the drug more frequently than once every 24 hours, it was occasionally given at 12-hourly intervals. The drug was given intravenously in doses of 7½ grains (0.48 g.) in from 10 to 20 c.c.m. of solution, injections being made very slowly (up to 5 minutes being taken for a dose). Oral administration was ineffective, and intramuscular injections were too painful. Although the drug was in some cases given almost daily over a period of months, no patient became aminophylline-fast. The authors pointed out the importance of preventing extravasation of the solution into the tissues, since intense burning may follow such an accident. In a considerable number of cases there occurred an initial hyperpnoea, a sensation of warmth especially in the face, spots before the eyes, a metallic taste, nausea, and vomiting. These reactions, though unpleasant, were never serious, and were generally transitory.

Continuous inhalation of vaporized broncho-dilator solutions.—D. W. Richards *et al.* described a continuous inhalation method suitable for severe asthmatic states. The method is also useful in such states as dyspnoea and chronic emphysema, and can be used with advantage in ambulatory and bed patients. The patient holds the nozzle of a vaporizer well within his oropharynx and breathes quietly for 3 to 10 minutes. One or 2 c.c.m. of a broncho-dilator solution, such as 1 in 100 adrenaline hydrochloride or 1 in 100 neosynephrine, are employed. The pulmonary function of the patients treated was investigated. There were no significant changes in pulmonary ventilation, but the vital capacity was increased in 26 cases investigated. Clinical improvement occurred usually with increase in vital capacity. An increase in maximal breathing capacity was an even better index of increased pulmonary function than an increase in vital capacity. The authors reported a case of status asthmaticus which responded to the continuous spray after other methods of treatment had failed. In 12 cases of chronic pulmonary disease 2 only received any

permanent relief from the continuous spray. One in 100 neosynephrine was found to be weaker in its action than 1 in 100 adrenaline, but could be used with safety for those who were sensitive to adrenaline

Treatment of Attacks

Adrenaline in oil—F. I. Keeney employed adrenaline in oil with good results in the symptomatic treatment of chronic and acute bronchial asthma. Twenty patients with chronic asthma received relief from symptoms for from 3 to 24 hours with from 0.5 c.cm. to 1.5 c.cm. doses. Forty-nine patients were treated during one or more attacks of asthma, each receiving from 0.5 c.cm. to 2.0 c.cm., 48 of these remained free from symptoms for from 4 to 24 hours, and one received more satisfactory relief from aqueous adrenaline than from adrenaline in oil. The injections were given subcutaneously in the upper arm, or intramuscularly in the deltoid or gluteal muscles. In all, 70 patients received 967 injections of adrenaline in oil.

'Slow' adrenaline—F. G. Dorwart reported a case of asthma treated with 'slow adrenaline' in arachis oil with alarming results. This preparation contained 2 mg. of powdered adrenaline in 1 c.cm. of peanut oil. The patient, a woman of 22 years, had had 3 previous attacks of asthma which had been controlled by injections of an aqueous solution of adrenaline hydrochloride. During the fourth attack she was given 5 minims of ordinary adrenaline solution and 1 c.cm. of 'slow' adrenaline in the right deltoid muscle. She quickly recovered from her asthmatic attack but was seized with a nervous restless feeling, as though she were going to die. Her respiratory rate was raised, her pulse irregular, and her heart sounds were very feeble. A tourniquet was applied to the right deltoid region to stop the flow of the adrenaline, and the patient became much better. When the tourniquet was released, owing to the condition of the arm and fingers, the symptoms returned and it had to be applied again. The patient was removed to hospital where she was treated with the tourniquet and by the administration of a 5 per cent dextrose in saline solution given intravenously. She gradually recovered and was discharged from the hospital about 3 hours later. On the next day the patient was normal. The cause of this reaction is unknown, but it was possibly due to the patient having a low tolerance to adrenaline. The author urged the necessity of using the 'slow' preparation with great care.

J. Cohn reported 3 cases of asthma treated with 0.25 c.cm. of a solution containing one part of adrenaline hydrochloride in 1,000 parts of saline followed half an hour later with 1 c.cm. of peanut oil containing 2.0 mg. of adrenaline crystals ('slow' adrenaline) injected intramuscularly. In these 3 cases complications such as cyanosis, vomiting, urticaria, and increased dyspnoea followed the second injection. A case of giant urticaria treated by the same method developed swelling and oedema of the forearm over the site of injection. This patient was later shown to be sensitive to peanut oil. Cohn concluded that, although this is a small series of cases, 'slow' adrenaline must be used with caution in the treatment of allergic conditions especially as the patient may be sensitive to peanut oil.

Cohn, J. (1939) *J. Allergy*, **10**, 459.

Dorwart, F. G. (1940) *J. Amer. med. Ass.*, **114**, 647.

Ffron, B. G., and Everett, P. (1939) *Med. surg. J.*, **92**, 77.

Keeney, F. I. (1939) *Amer. J. med. Sci.*, **198**, 815.

Richards, D. W., Jnr., Barach, A. L., and Cromwell, H. A. (1940) *Amer. J. med. Sci.*, **199**, 225.

ATHLETICS AND ATHLETIC INJURIES

See also B. E. M. P., Vol. II, p. 220, Cumulative Supplement, Key Nos. 114 and 115; and Surveys and Abstracts, 1939, p. 235.

Athletics

The Heart and Sport

The circulation in athletes—H. J. Stewart and R. F. Watson measured the arterio-venous oxygen differences, oxygen consumption, minute-volume output of the heart, vital capacity, cardiac size, circulation time, venous pressure, arterial pressure,

and heart rate in a group of 14 healthy male athletes, between the ages of 19 and 23, all of whom were members of a college football team and had been engaged in competitive school and college athletics for periods of 2 to 9 years. Similar measurements were made in a control group of 11 healthy males between the ages of 19 and 29, who were engaged in sedentary occupations, and who took only occasional mild athletic recreation. These measurements were carried out under basal conditions. There was no significant difference between the findings in the two groups, with the exception that the stroke volume of the athletes was slightly larger. This difference appeared to be related to body size, since the stroke volume per kilogram of body weight, and the cardiac index for the two groups were approximately the same.

Acute Fatal Non-traumatic Collapse during Exertion

F. Jokl and L. Melzer critically analysed 21 among 6,370 necropsies made at the South African Medico-Legal Laboratories, Johannesburg, between 1934 and 1939, and also 43 collected cases, all examined after death, of acute fatal non-traumatic collapse during work or sport, in order to ascertain if physical strain can cause fatal collapse due to morbid processes previously unrecognized. Heat stroke is not included and it is stated not to have been reported in an athlete (compare B. E. M. P., Vol. II, p. 225). In practice the problem of fatal collapse during or after physical exertion or sport is difficult, because many persons have well-marked cardiovascular diseases without their knowledge, and a number of cases among prominent athletes are given to emphasize the conclusion that the degree of 'fitness', as measured by athletic efficiency, is not a reliable indication of the presence or absence of organic disease of the circulatory system. There was not among the 64 cases analysed any example of a previously healthy person dying suddenly from excessive exertion. In all the cases the cause was one or more of the following diseases of the cardiovascular system: coronary arterial disease, aortic aneurysm, disease of the cerebral or pulmonary arteries, myocardial inflammation or degeneration, rupture of the heart or aorta. This conclusion confirms previous publications by Jokl.

Jokl, F., and Melzer, L. (1940) *S. Afr. J. med. Sci.*, **5**, 4.

Stewart, H. J., and Watson, R. I. (1940) *J. clin. Invest.*, **19**, 35.

Athletic Injuries

Treatment of Knee-Injuries

End results.—F. S. Hopkins and L. L. Huston analysed the end-results of the treatment of 193 cases of knee-injuries sustained by athletes. Most of these cases were simple synovitis and 81 per cent of them showed good final results. In the treatment of semilunar cartilage injury, immobilization in plaster was found to give superior results to treatment with bandaging, physiotherapy, etc. Conservative treatment in these cases was so satisfactory, nearly half being cured, that Hopkins and Huston considered that it should always be tried before surgery is resorted to. The remainder of the cases, which still had adverse symptoms, gave good results (66 per cent) on treatment, and all of them were sufficiently improved by operation to take part in athletics again.

Hopkins, F. S., and Huston, L. L. (1939) *New Engl. J. Med.*, **221**, 95.

AVIATION

See also B. E. M. P., Vol. II, p. 239, Cumulative Supplement, Key No. 116; and Surveys and Abstracts 1939, p. 236.

Examination of Pilots

Examination of the Special Senses

The labyrinth.—W. Salem has about 200 reports of airmen examined for the soundness of their labyrinthine apparatus. The labyrinth is not the only organ of equilibrium but is the most important one and it should function perfectly in airmen. The author, however, distinguishes between an aviation candidate in whom there should be a rigorously strict examination and an experienced airman in whom the examination need not be as strict because the airman can compensate some defects of the labyrinth by his experience.

In an aviator the organs, especially the labyrinth, become easily tired. The labyrinthine excitability also diminishes with increasing age. Labyrinthine examinations cannot be calculated by algebraic formulae and isolated signs are of no clinical value. The author uses the rotatory chair only for aviation candidates and not for experienced airmen. He does not use the 'rolling chairs'. He uses the caloric examination in Brunings' third position or with the head vertical, following Isaac Jones. The examination may show hypo-excitability, hyper-excitability, or a normal labyrinth. The interpretation of the stages is: (i) Hypo-excitability. A practised pilot very often has a diminished excitability, as have dancers and acrobats. This is an occupational hypo-excitability without clinical importance, especially in pilots who have done a great deal of an acrobatics. (ii) Hyper-excitability. If long aerial practice diminishes the excitability of the labyrinth, violent efforts increase it. The examination itself is often a cause of hyper-excitability. The author concludes that each case should be judged on its merits.

Salem, W. (1939) *Pr. méd.*, **47**, 1191.

Diseases Associated with Aviation

Amniosis Luxa ('Blacking out')

R. B. Phillips and C. Sheard discussed 'blacking out', the condition which occurs in aviators during a sudden change of direction when flying at high speed. During flying the unit force of gravity (g) may be increased 9 or more times so that the pilot and his plane are subjected to this greater force. Acceleration in an aeroplane may be linear, in a curved path, or angular. Angular acceleration produces little effect upon the pilot except possible vertigo. Linear acceleration up to 6g produces only a feeling of pressure on the body. From 6 to 8g inspiration becomes difficult. Acceleration in a curved path produces a negative centrifugal force (head away from the centre of the circle) or a positive force (head towards the centre of the circle). When the force is acting from head to feet at about 5g there is loss of muscular control and blood leaves the head space, leading to a diminution or complete loss of vision. After 5g there is loss of sensory functions and between 6 and 9g coma appears. Usually, when acceleration is decreased, consciousness returns and sight is restored. There is a short latent period after the acceleration before the development of the pressure changes. The length of the blacking-out varies in different individuals, as does the amount of g necessary to produce symptoms, and the symptoms produced. The primary cause of the blackout is that the blood leaves the brain and not that the central retinal artery is compressed. There are a few methods of combating blackout. Among them are shouting loudly when diving, tensing the muscles of the abdomen and the legs, and leaning forward just when coming out of a dive to convert the force as nearly as possible to a transverse one.

Phillips, R. B., and Sheard, C. (1939) *Proc. Mayo Clin.*, **14**, 612.

Effect of Aeroplane Noise on Hearing

I. D. Dalziel Dickson *et al.* describe the effects of aeroplane noise on the auditory acuity of aviators. If the ears are unprotected the pilots become deaf to the higher tones, men working on the ground with noisy machinery are similarly affected. This loss of hearing occurs early in flying experience, and is at first temporary only; it is greatest in the ear nearer the engine, and tinnitus may also be present for some time. There is loss of bone- and air-conduction for the frequencies of the high notes affected. Analysis, however, of the noise from aeroplanes shows that the loudest noises are at low frequencies. Since protection of the ears lessens the incidence of deafness, investigation of various methods was undertaken. Packing the ears with various substances, such as vaseline and plasticine, was tried, but it is very difficult to make the substance fit the meatus properly; on the whole, a flying helmet, firmly strapped to the ears, gave the best protection. The effect of the noise of the engine on the ears has been found to be less severe when the pilot sits well forward in the place in front of the engine.

Dickson, I. D. D., Ewing, A. W. G., and Littler, T. S. (1939) *J. Laryng.*, **54**, 531.

BACKACHE AND LUMBAGO

See also B.E.M.P., Vol. II, p. 251, Cumulative Supplement, Key No. 117, and Surveys and Abstracts 1939, p. 238

Abnormalities*Sacralization of the Fifth Lumbar Vertebra*

Diagnosis and treatment —F. Stefani discussed partial sacralization of the fifth lumbar vertebra, a condition which causes pain in the lower extremity and backache, without any lesion of the cord. The pain is due to pressure and irritation of the sensory nerves. Sensitivity and motor function in the lower extremity are normal. The injection of 10 c.cm. of procaine hydrochloride (novocain) is a good method of proving this to be the cause of the condition, as lumbosacral pain from any other cause is not relieved in this way. The operative treatment of the condition, which is advisable in longstanding cases, is resection of the macro-apophysis.

Stefani, F. (1939) *Chir. Organ. Mov.*, **24**, 565.

BILHARZIASIS

See also B.E.M.P., Vol. II, p. 323, and Surveys and Abstracts 1939, p. 240

Morbid Anatomy

A. S. Price describes the parasitology, morbid anatomy, clinical picture, and diagnosis of urinary schistosomiasis. Important points are its division into 3 groups: (1) local lesions in the genito-urinary tract due to the adult parasite in the veins of the urinary bladder and the adjacent area, (2) general visceral lesions due to the presence of the adult parasites and their toxins, and (3) local and systemic lesions due to the presence of ova in the tissues. Locally, in addition to the haematuria and pain, there may be purulent cystitis. The only satisfactory means of diagnosis is the presence of ova in the urine sediment.

Price, A. S. (1940) *Urol. cutan. Rev.*, **44**, 56.

BLADDER DISEASES

See also B.E.M.P., Vol. II, p. 374, and Surveys and Abstracts 1939, pp. 34 and 242

Nervous Disorders*Vesical Neuralgia*

Aetiology and treatment —L. Crisploti discussed the treatment and aetiology of vesical neuralgia, a condition characterized by pain, tenesmus, and dysuria, the pain is not relieved by menstruation. The clinical condition often resembles an acute abdominal emergency, such as acute gall-bladder disease, appendicitis, or acute kidney disease. The cause is a neuritis of the pelvic sympathetic nervous system. The treatment is removal of the upper hypogastric plexus and division of the sacral sympathetic; rapid cure usually follows.

Crisploti, F. (1939) *Ginecologia*, **5**, 521.

Lichen Planus

F. I. Young reports a case of lichen planus of the bladder. Skin diseases may attack the mucosa of the bladder in the same way as they sometimes involve that of the mouth and rectum. The patient, a man aged 21 years, complained of slight urethritis and burning on micturition. The urine contained blood and pus. No pathogenic organisms, except staphylococci, were found, and the patient attributed his condition to indiscretions in diet and drinking. He had had a previous attack, during which an area of lichen planus on the skin flared up. This was not at first associated with the bladder condition. The patient recovered on rest and palliative

treatment, but further attacks followed, each accompanied by an exacerbation of the lichen planus. Cystoscopy showed a generalized cystitis with elevated reddened areas on the postero-lateral wall of the bladder. Only 2 other similar cases have been reported.

Young, I. L. (1940) *J. Urol.*, **43**, 265.

Cystitis

Treatment

Sulphanilamide—L. A. Ranty and C. S. Keefer employed sulphanilamide in 17 cases of infection of the urinary tract due to *Bact. coli*. In most cases clinical improvement and sterilization of the urine occurred. The urine could generally be sterilized by the administration of 2 to 5 g. of sulphanilamide, by mouth, in 24 hours, this dosage effected concentrations of from 23.0 to 139.0 mg. per 100 c cm. of urine. The best results were obtained in cases in which there was no previous history of infection of the urinary tract, and in those in which the infection was associated with pregnancy. When there was evidence of chronic infection of the urinary tract, the urine was difficult to sterilize, and clinical and bacteriological relapse frequently occurred.

Ranty, I. A., and Keefer, C. S. (1940) *Arch. intern. Med.*, **65**, 933.

Neoplasms

Malignant Growth

Treatment super-voltage x-irradiation—I. H. Colby reports on the use of super-voltage X-rays in 8 cases of malignant tumour of the bladder. The apparatus employed was a one million volt X-ray generator recently installed at the Huntington Memorial Hospital, Boston, Mass. The technique employed was as follows: A daily dosage of 400 r was given alternately to the anterior, left posterior, and right posterior pelvis, the exposure time was 5 minutes, 45 seconds; current 1.2 milliamperes, filtration through 5 mm. lead, half value layer of copper, 11 mm., focal skin distance 70 cm. The total dosage varied from 5,600 to 16,800 r. Of the 8 patients treated by this method, 5 had not undergone previous treatment, 2 had received electro-coagulation with permanent cystotomy, and, in one fulguration had been done 12 years previously and open operation 10 years subsequently. After super-voltage radiation 2 patients showed marked regression of the tumour; in 2 patients there was considerable or marked intravesical regression, and in 1 patient relief of symptoms with apparently some regression of the tumour, but in 3 patients there was little or no symptomatic relief. In conclusion, bladder tumours appeared to be definitely affected by super-voltage irradiation, the portions of such tumours projecting into the bladder cavity showing much more regression than those which extended into the bladder wall. Local and general reactions were much less than with lower voltages, with circumscribed malignant vesical tumours operation was advisable, and super-voltage irradiation was recommended only when the growth was too extensive for operation. Further experience was necessary before a proper evaluation of the method could be made.

Colby, F. H. (1939) *J. Urol.*, **42**, 538.

Post-Operative Retention

Bacteriology

L. K. Stalker and T. L. Schulte examined the urine of 73 patients who were being catheterized for post-operative retention. In 39 cases no symptoms of urinary infection developed, and in 31 of them urinary cultures were persistently negative. In the remaining 8 cases only a few colonies of organisms were present, and the urine was sterile at the time of dismissal, although no therapy was given. A retention catheter was used in 4 of these 39 patients, and the rest were treated with intermittent catheterization. In the 34 other cases symptoms of urinary infection developed, although the urinary culture was positive in only 32 of them. In those

treated with intermittent catheterization the culture became positive approximately after the ninth treatment. When a retention catheter was used the cultures became positive soon after its insertion. Residual urine developed in 16 cases, and the amount was always greatest when the symptoms of infection were most numerous. All these cases of urinary infection cleared up with appropriate treatment. Because infection of the urine often develops quickly after a retention catheter has been inserted, a group of 11 cases, in which one had been inserted at the time of resection of the rectum, were given sulphanilamide as a prophylactic. The drug was given subcutaneously on the first few post-operative days as a solution containing 12.5 g. per litre. When it could be taken by mouth 5 g. were given 3 times daily. The catheter was left in for an average of 8.5 days. The urine was sterile in 3 cases and in the others only a few colonies of organisms resulted and they did not produce symptoms of infection of the urinary tract. It was concluded that sulphanilamide is a good prophylactic against urinary infection in cases of post-operative retention, but that it should be used with caution because of the possibility of toxic symptoms developing.

Stalker, L. K., and Schulte, T. L. (1939) *Proc. Mayo Clin.*, **14**, 730.

Surgery

Transplantation of Ureters

C. Morson and W. H. Graham reported on the results obtained from transplantation of the ureters into the large bowel in 13 patients, comprising 1 case of tuberculous bladder, 6 of carcinoma of the bladder, 1 of carcinoma of the cervix with invasion of the trigone, 1 of complete procidentia with vesical calculi, 2 of complete incontinence, 1 of systolic bladder due to chronic sepsis, and 1 of vesico-vaginal fistula due to carcinoma of the cervix and vagina. The most striking feature in this series of cases with regard to the immediate results was that no deaths occurred among the non-malignant cases, whereas 5 of the malignant cases died. With regard to immediate results of operation there was very little reaction or shock. About 36 hours after operation urine was excreted rapidly and in increasing volume. After the first 5 days convalescence was apyrexial. Frequency of bowel action varied considerably, all cases becoming continent within 10 days of operation. After that period most of the patients developed such control that they could discriminate between the expulsion of fluid, faeces, and flatus.

Morson, C., and Graham, W. H. (1940) *Brit. J. Surg.*, **27**, 540.

BLASTOMYCOSIS

See also B.F.M.P., Vol. II, p. 403.

Disseminated Blastomycosis

L. J. Solway *et al.* of Toronto report, with illustrations of the viscera, a case of widely disseminated blastomycosis in a man, aged 48. Clinically the onset with cough, weakness, some fever, and loss of weight was gradual and at first suggested pulmonary tuberculosis. Later the clinical diagnosis was blastomycosis affecting the lungs, liver, spleen, epididymis, spinal cord (transverse myelitis), and terminal invasion of the skin and skeleton. Biopsy showed the presence of *Zymonema dermatitidis* (*Blastomyces gilchristi*). X-rays showed that both lungs were invaded by miliary lesions the size of a pin-head and others the size of a pea and larger than miliary tubercles, and some with translucent centres and a tendency to conglomeration. Large doses of sulphanilamide were given, but without any benefit. The necropsy confirmed the diagnosis made during life.

Solway, L. J., Kohan, M., and Pritzker, H. G. (1939) *Canad. med. Ass. J.*, **41**, 331.

BLINDNESS

See also B E M P, Vol II, p 407, and Surveys and Abstracts 1939, pp 128 and 244.

Inflammation*Syphilitic Primary Optic Atrophy*

Tryparsamide therapy S F C. Turvey reported the results obtained from the use of tryparsamide in 15 cases of primary optic atrophy due to syphilis. In 9 cases there was improvement in visual acuity, in 4 the visual failure was arrested for periods varying from 6 months to 2 years, and in 2 the drug was probably harmful. Injections of the drug were given weekly in doses of 1 g., 1 g., 2 g., 2 g., and then 6 to 8 injections of 3 g. each. After an interval of 1 to 3 months a similar course was given. The visual acuity, the perimetric fields of vision, and the fundi were carefully examined before treatment was begun, and the visual acuity and confrontation fields for colour were tested before each injection. All but 2 of the patients received 20 or more injections of the drug, and all but 3 had received malaria therapy. Since the period of observation was not long enough, and because most of the patients had had malaria therapy, the author could not state that tryparsamide produced all the good effects, but he suggests that the drug is not contra-indicated in certain selected cases of syphilitic optic atrophy.

Turvey, S F C (1940) *Canad med Ass J*, **42**, 264

BLOOD EXAMINATION

See also B E M P, Vol II, p 457, Cumulative Supplement, Key Nos. 163-169, Surveys and Abstracts 1939, pp 21, 52 and 245, and pp 113, 119 and 137 of this volume.

Blood-Grouping*Rapid Method of Cross-Agglutination and Syphilis Test*

A. H. Walters evolved a rapid technique for blood-grouping and a rapid method of cross-agglutination and syphilis test for the donor. Agglutination tests for donors are done on an agglutinator by mixing a drop of the donor's citrated blood with a drop of group-A serum and a drop of group-B serum, and after mixing reading the result, positive agglutination showing up as large coarse red folliculi. The recipient's blood is grouped in the same manner, having first been diluted with sodium citrate. The haemoglobin percentage is divided by 100 and the answer gives the number of parts of blood in ten parts, the rest being made up in sodium citrate. Cross-grouping can be carried out on the agglutinator between the recipient and donor, if there is time.

Laughlin's reagent is used in the test for syphilis. It is activated by dilution with saline and standing at room temperature for 24 to 48 hours. A drop of donor's serum placed in a water bath at 63° C. for 3 min. is then placed on the agglutinator with 0.2 c.c. of the reagent. They are rotated for 5 minutes and then examined for red floccules. They are then rotated for a further 9 minutes and examined again. After the first 5 minutes they can be mixed with a needle if no floccules have appeared. Coarse red floccules indicate a strongly positive reaction and fine ones a weak or doubtful reaction. Walters has found this to agree within 98 per cent with the Kahn test, but he considers that the Kahn test should be performed later, and always in doubtful cases.

Walters, A. H. (1939) *Lancet*, **2**, 831.

Coagulation*Bleeding-Time*

New method of determination H A L v. Dishock and L B W Jongkees described a new method of determining bleeding-time. The ear is made hyperaemic by rubbing. It is then pressed against a thin steel plate, e.g. a razor blade, with a

circular opening 4 mm. in diameter. A small part of the lobe is protruded through this opening, and cut off with a razor. Thus, an open wound is obtained in which many capillaries have been cut. The wound should preferably not be made on the edge of the lobe. The blood is sucked up every half-minute with a separate piece of filter-paper, without the wound being touched, and the number of drops on the paper indicates the bleeding-time in half-minutes. The force with which the ear lobe is pressed against the steel plate can be made constant by fastening a steel spring to the plate and fixing the lobe in between. To test the value of this method the authors determined the bleeding-time of 85 people, in each case this was done twice with an interval of 4 hours. The average bleeding-time in 450 tests was 3 minutes, 25 seconds. With Duke's method, an average bleeding-time of only 2 minutes, 30 seconds was obtained. With the authors' method haemorrhage is not hindered by the edges of the wound adhering together through tension of the tissues.

Dishock, H. A. E. v., and Jongkees, L. B. W. (1940) *Lancet*, **1**, 692

Platelet Count in the New-born

I. G. Hodge examined the blood of the umbilical cord of 16 infants, and found the average platelet count per cubic millimetre to be 278,000 with extremes of 380,000 and 205,000. These figures are in closer agreement than many previously reported, namely 95,000 to 1,092,000. The extremes in counts must be due to errors in technique. It was found that clumping of the platelets in the counting chamber could be avoided by allowing the blood from the cord to flow freely before a specimen is taken and by immediate counting.

Hodge, I. G. (1939) *Bull. Amer. Clin. Lab.*, **Phila.**, **3**, 277

BLOOD-PRESSURE, HIGH AND LOW

See also B. F. M. P., Vol. II, p. 503. Cumulative Supplement, Key Nos. 170 and 171, and Surveys and Abstracts 1939, pp. 19, 56 and 248.

High Blood-Pressure

Essential Hypertension

Aetiology. S. W. Mulholland discusses the problem of hypertensive disease, especially its renal origin, in an article with 63 references to work such as that of Goldblatt. He divides hypertensive diseases into (i) cases caused by local inflammatory, suppurative, or obstructive impairment of one or both kidneys, in cases in which infection has caused diminution of the renal blood flow, nephrectomy has been followed by a reduction of the high blood-pressure. (ii) essential hypertension, in this condition hypertonus of the efferent glomerular arterioles has been thought to cause renal ischaemia, and Paunz has shown experimentally that a new blood-supply can be provided to the kidney by omentopexy, and possibly this may in the future be adapted to practice. Reference is made to Crile's suggestion that renal decapsulation should be performed as an adjunct to coeliac ganglionectomy.

S. J. G. Nowak reports the production of chronic hypertension in dogs by excision of the carotid bifurcation and of the cervical aortic-depressor nerve. Hypertension had lasted as long as 3 years and 4 months, fluctuating from time to time, but it was not influenced by pregnancy in one dog. The hypertension produced by these operations was not accompanied by any changes in blood chemistry or in the urine. Nerve resection unaccompanied by excision of the carotid bifurcation did not result in a lasting elevation in the blood-pressure. This method was successful in 4 dogs, whereas the first method failed in 4 dogs. Two of these dogs showed that some degree of aortic-depressor nerve activity was still present. The anaemia produced by the excision of the carotid sinus varied, and was proved not to be the cause of the hypertension. Tachycardia usually accompanied the rise of blood-pressure in the dogs and varied directly with it.

Presence of a urinary precursor principle. I. J. Jones reports the case of an athletic man, aged 26, with achlorhydria and macrocytic anaemia responding to liver

treatment, who was found to have a blood-pressure of 190/110 mm. Hg without renal disease. The association of hypertension and anaemia suggested that there might be a common origin in overactivity of the posterior pituitary. This possibility was rendered more probable by a grossly-abnormal blood-sugar curve. The blood and urine were then extracted for pituitrin; the blood extract was negative on the two occasions when it was tested, the urinary extract was injected into a spinal cat and gave a well-marked pressor response, the curve being identical with that given by pituitrin. The urine was thus repeatedly examined for 6 months and on every occasion was positive for the pressor substance, except one when it was strongly alkaline and may have destroyed it. But towards the end of the 6 months the amount of the *pituitrin-like pressor substance in the urine had gradually diminished* and at the same time the blood pressure returned to normal. The patient's urine was also found to contain an anti-diuretic principle, though he was passing urine normally, and thus appeared to have become resistant to it. An extract of the patient's urine caused definite melanophore dilatation in frogs, whereas an extract of normal urine had not any effect on control frogs. The urine of 8 other hypertensives was later examined, in 5 no trace of the pituitrin-like pressor substance was found, the 3 other urines gave a positive response to the pituitrin-like pressor substance and also to the melanophore dilatation test. The author suggests that some cases of hypertension may be due to overaction of the posterior pituitary.

Heredity.—E. A. Hines, Jr., reports on the presence of hypertension among 1,374 patients treated at the Mayo Clinic 10 or 20 years ago, who answered questions then about their family history, but had not then been hypertensive. In both the 10-year and 20-year groups the incidence of subsequent hypertension was approximately 6 times higher among those with a positive family history than among those with a negative family history. Among 58 who stated at their original visit that both parents were hypertensive, 52, or 89.6 per cent, were hypertensive when examined 10 or 20 years later. From earlier investigations of the reaction of the blood-pressure to the cold pressor test, the author concludes that those who usually have a normal blood-pressure, but give a positive reaction to the cold pressor test, are pre-hypertensive individuals and many of them will eventually become hypertensive.

Carbon monoxide poisoning.—M. Staemmler and G. W. Parade reported the case of a man who, at the age of 42, had a blood-pressure of 225/140 mm. Hg. This man had repeatedly inhaled small quantities of carbon monoxide. At the age of 48 he died, and at necropsy there was found at the periphery of the internal capsule and lenticular nucleus an old yellow centre of softening, while the adrenal medulla was greatly hypertrophied. The authors concluded that the carbon monoxide had caused excessive secretion of adrenaline and medullary hypertrophy, with consequent increased blood-pressure, or that chronic stimulation of the adrenals resulted from changes in the brain.

Relation to renal injury in pyelonephritis.—In a case of bilateral post-partum pyelonephritis in which one kidney was removed at the height of the infection, and the other apparently recovered, L. G. Crabtree and F. I. Prien report evidence of damage to the arterial blood supply in most parts of the intact kidney. It was considered that infective lesions in the arteries supplying the renal cortex should be taken into account as a possible cause of hypertensive renal disease. Clinical observation of 30 cases of severe bilateral pyelonephritis in pregnancy at from 10 to 18 years after the initial infection, showed that only 2 of these patients were hypertensive, but renal function tests in 7 of these cases showed that all had severe degrees of renal injury. Hypertensive tendencies in these cases were not proportional to the degrees of renal deficiency demonstrated at this stage of the natural history of the disease. Hypertension was not the rule in severely injured kidneys due to pregnancy pyelonephritis even remotely (10 years) after the initial injury in patients who showed reasonable degrees of health. This does not indicate whether or not these patients might not become hypertensive late in life, but suggests that there may be in some, but not in all, a remote relation of cause and effect between hypertension and severe pyelonephritis. There is not yet, however, sufficient evidence to justify radical departure from present conservative renal surgery.

Pathology and pathogeny.—P. Rimbaud and A. Delmas report the case of a man, aged 57, who normally had a systolic blood-pressure of 140 and a diastolic of 100 mm. Hg, but had paroxysmal crises of blood-pressure 220-290 systolic and 140-130

diastolic mm. Hg. Necropsy showed a large cortical adenoma of the left adrenal which weighed 19 g. (normal 7 g.) with much abnormal hyperplasia and altered structure of the zona fascicularis and spongiocytic proliferation. The right adrenal was not macroscopically enlarged, but microscopically showed adenomatous spongiocytic change. This case therefore showed the same paroxysmal crises of hypertension known to occur in cases with chromaffin-called tumours (phaeochromocytomas, chromaffinomas, paragangliomas), but in this there was not any such change.

Effect of blood-pressure on subsequent course - H. Gross and H. Engelberg analysed 100 cases of hypertension and severe coronary artery disease, examined at necropsy, to discover the effect of blood-pressure on the subsequent course. Ninety cases had chronic congestive heart failure, which frequently followed an acute coronary occlusion. There were 24 cases with terminal acute coronary closure, 15 of these had hypertension up to the final closure, 7 had low blood-pressure for several months before closure, and in 2 the blood-pressure had varied in the preceding year. Subsequent to the acute coronary occlusion, 18 had persistent hypertension, 12 had permanently low blood-pressure, and in 10 the pressure varied. Of the cases, 21 had died suddenly, many having the clinical picture of acute coronary thrombosis. The subsequent blood-pressure in hypertensive cases following coronary thrombosis had no effect on longevity, or on the occurrence, severity, and duration of heart failure. Neither was there a definite relation between the course of blood-pressure and the heart weight and the duration of failure.

Potassium thiocyanate therapy - R. W. Robinson and J. P. O'Hare reported the results obtained from the use of potassium thiocyanate in 75 cases of hypertension, all of which were ambulatory. The drug was administered as a 5 per cent solution in syrup of wild cherry. Most patients received first 3 doses of 0.2 g. of the drug (4 c.cm. of the solution) daily for 3 days. The dosage was then reduced to twice daily for the rest of a week. At the end of this time the patients were examined, specific enquiries being made as to toxic symptoms, and the blood-pressure was taken. A sample of blood was examined for cyanate concentration, and, if there were no toxic symptoms and no fall in blood-pressure, treatment was continued with 2 doses daily. Thereafter the dosage was regulated by the blood-cyanate and blood-pressure levels. Patients were seen approximately once a week during the first 6 or 8 weeks of treatment, or until the blood-pressure had fallen to an optimal level and the blood-cyanate remained at a fairly constant concentration without toxic symptoms. When this stage was reached the intervals between visits was increased to 2 or 3 weeks. It was found that some patients required only 0.2 g. 3 times a week, while others required as much as 1 g. a day to obtain a good response at a satisfactory cyanate level. In 3 cases maximal drops in blood-pressure of over 100 mm. Hg systolic and 35 mm. Hg diastolic were observed. An average drop of 40 mm. Hg systolic and 20 diastolic occurred in 63 per cent of cases. The effects noted were chiefly relief of headache in 18 out of 20 cases. Toxic symptoms occurred in 29 cases; the less serious toxic complications accounting for 23 of these 29 cases were weakness, nausea, dermatitis, purpura, and a decrease in libido. Serious complications, which occurred in 6 cases, were dermatitis exfoliativa, congestive heart failure, cerebral thrombosis, angina pectoris, and psychoses. The authors concluded that thiocyanate therapy had decided value in uncomplicated vascular hypertension in patients under 60 years of age.

Acetyl- β -methylcholine therapy - D. F. Engle and M. W. Binger investigated the response in blood-pressure of hypertensive patients to acetyl- β -methylcholine. They stated that arterial hypertension in man was due to increased peripheral vascular tone. This increased tone might be due to failure of the vasodilator mechanism which is possibly insensitive to such vasodilators as acetylcholine or protected from its action by some atropine-like substance. They therefore compared the action of the derivative acetyl- β -methylcholine in hypertensive and normal subjects. Subcutaneous injections of 2.5 mg. were given in both groups. They found that the peripheral vessels of the hypertensives were more dilated by the drug than those of the normals. Moreover, the reflex vasoconstriction of the hypertensive to cold was reduced after the administration of acetyl- β -methylcholine. The drug produced a greater lowering of blood-pressure in the hypertensive than did deep anaesthesia with pentothal sodium. The diminution of blood-pressure during deep

anaesthesia is due to the almost complete abolition of vasoconstrictor control. That vasodilatation was not complete in these circumstances was shown by its further lowering on giving a vasodilator drug. The authors concluded that, since hyperdilatation is produced in hypertensives by this drug, it is difficult to believe that the peripheral vessels are in a state of increased tone unless the concentration of acetylcholine at the nerve endings is deficient in these subjects.

Sulphur therapy. M. Loeper and J. Parrod consider that sulphur is often of more value than iodine in arterial disorders and diseases. Cartilage is the tissue in the body richest in sulphur, and the walls of the arteries come next. Sulphur exerts a trophic action on the arteries, preserves elasticity and contractility, and prevents the deposition of calcium and cholesterol. Patients with atheroma have improved after taking sodium hypsulphite. Animals with a raised blood-pressure due to the intravenous injection of tyramine showed a reduction after the administration of sodium hypophosphite, and a number of hypertensive patients have been given intravenous injections of the sulphur salt with a slow progressive fall of pressure. Sulphur does not, it is thought, directly lower the pressure, but acts by uniting with hypertension bases with the production of non-tensive bodies, such as tyramine sulphuric acid.

X-ray therapy. J. H. Hutton writes on the influence of the endocrines in essential hypertension. Being convinced that some functional abnormality of the pituitary and adrenals is responsible for many cases of hypertension, he applied small doses of irradiation to these organs. Among 277 patients adequately treated, 191 (68.95 per cent) improved, but of these 191, 29 (10.47 per cent) relapsed, whereas 162 (58.48 per cent) maintained the improvement. Of the total number of patients, 86 (31.04 per cent) did not improve. Whilst the treatment does not entirely correct the cause, and must be repeated at varying intervals, it can keep the patient practically free from symptoms, and is harmless.

Treatment surgical. I. Davis and M. H. Barker discuss the surgical treatment of hypertension. Of 200 cases success followed thiocyanate treatment in about 50 per cent. In 25 per cent the initial response was good, but it could not be maintained. The remaining patients were resistant to cyanate treatment and the authors therefore considered surgical treatment. All these patients had very high blood-pressures, over 200 mm. Hg systolic and 100 mm. Hg diastolic. There was no evidence in any of them of renal damage or marked arteriosclerosis. These patients were comparatively young, one reported case being only 25 years of age. In 4 patients section of the splanchnic nerves above the diaphragm was performed, although this procedure failed to lower the blood-pressure, these patients became susceptible to cyanate treatment. This may be due to the vasodilatation following operation allowing the drug to act more readily. The vasodilatation may also clear the blood of the cyanate more quickly so that it does not reach a toxic level before it begins to act. The authors reproduced the results experimentally in hypertensive dogs. The action of potassium thiocyanate in hypertension is unknown, but may be due to an increase in the permeability of the capillaries causing the pressure to fall.

P. B. Ascroft reviewed the possible cause of essential hypertension. The high blood-pressure is maintained by arterial and arteriolar constriction which is under chemical and not nervous control. Experimentally the chemical substance was found to be of renal origin and is known as renin. Ascroft discussed the surgical treatment of hypertension and concluded that of all those tried at present wide splanchnic denervation gave the best results. It is, however, only useful in certain cases in which the blood-pressure is still labile and can be influenced by rest and medical treatment. Even in these cases a good result is not certain. On the assumption that renin is destroyed and therefore made inactive by the normal kidney it was suggested that improving the blood supply to the hypertensive kidney would result in a fall of blood-pressure. Experimenting with animals Goldblatt found that constriction of the renal artery produced a lasting high blood-pressure, but if the kidney were first decapsulated and muscle or fat with a high blood content was grafted on to the denuded area, the rise in blood-pressure was not permanent. From these observations it was concluded by Ascroft that nephro-omentopexy may be of use in the surgical treatment of hypertension as the omentum has great powers of vascularization.

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High Blood-Pressure in General

Aetiology

Prevention of hypertrophy of the kidney—Following Goldblatt's demonstration that constriction of one renal artery causes a transient rise of blood-pressure which is made permanent by removal of the other kidney, W. F. Greenwood *et al.*, of the Physiological Department of Toronto University, experimented to see if, by prevention of the compensatory hypertrophy of the remaining kidney which normally follows removal of one kidney, hypertension was produced. The exposed kidney was enveloped with strips of gauze soaked in collodion and allowed to harden, a layer at a time, in situ, after hardening, a window $\frac{1}{2}$ to $\frac{3}{4}$ inch square was made in the cast opposite to the hilum, the dog's normal blood-pressure was established before the cast was made, and 5 to 10 days after the cast was made the other kidney was removed. In 6 dogs which did not show any rise of blood-pressure after the first operation, the nephrectomy was followed by a pronounced and rapid rise of blood-pressure which appeared to be permanent. Three dogs in which both kidneys were enclosed in casts, with or without windows, all died in uraemia in 4 days without any rise of blood-pressure.

Prognosis

J. A. Ryle, who prefers Allbutt's term hyperpiesia, divides the individual cases into 5 groups for the purpose of prognosis: (i) men, 45-50, with a blood-pressure of 170/100 mm. Hg, without symptoms and without arteriosclerosis and albuminuria may survive for 15 or more years, and may continue normal activities for 5 or more years, (ii) with a blood-pressure of 200/110, slight symptoms referable to the head or heart, slight albuminuria, arteriosclerosis and cardiac hypertrophy, there may be an interval of 5 years before late sequelae follow, and survival lasts for no longer than 10 years, (iii) blood-pressure 220/120, with minor vascular accidents, such as retinal haemorrhages, transitory aphasia, lesser-grade coronary thrombosis, and effort angina, there is hyperpiesia with arteriosclerosis, and early structural damage to viscera, survival is not likely to exceed 5 years, (iv) blood-pressure 240/130, gross vascular lesions, such as cerebral haemorrhage or thrombosis, and coronary thrombosis, or congestive heart failure, there is hyperpiesia with arteriosclerosis and serious structural damage to viscera, survival generally does not exceed 1 or 2 years, (v) the patient is bedridden with chronic heart failure, hemiplegia, or mental deterioration from wide-spread arteriosclerosis. The systolic blood-pressure may fall but the diastolic remains high 190/140. Survival is a matter of days, weeks, or at the most months.

The prognosis of so-called 'malignant hypertension' corresponds with that of the fourth or fifth stages of the more chronic or gradual form of the disease. The outlook in menopausal patients is much better than that in men of the same age, and progress to the stage of arteriosclerosis is less likely to occur.

Nature of Peripheral Resistance

L. A. Stead, Jr., and P. Kunkel discuss the question whether the high average arteriolar resistance which is present throughout the body at rest in arterial hypertension can be reduced to normal in any one tissue by the use of appropriate local vasodilating agents. An investigation was carried out on 16 patients with arterial hypertension, their average age being 43 and the average systolic pressure 206 mm Hg. It was found that the increased peripheral resistance present in arterial hypertension cannot be reduced to normal level in the skin of the hand and foot, the muscles of the forearm, or in the brain by powerful vasodilating stimuli. The finding of a uniform degree of elevation of the peripheral resistance throughout the body militated strongly against the neurogenic origin of the usual types of clinical hypertension, because the nervous vasomotor control was different in each of the tissues investigated.

Cold-Pressor Reaction

J. H. Miller and M. Bruger studied the blood-pressure responses to a standard cold stimulus, using a recording sphygmomanometer, in a group of 89 persons, comprising normal subjects, hyper-reactor normal subjects, patients with nephritis with and without hypertension, and patients with essential hypertension. It was found that 39 per cent of the normal subjects and 76 per cent of the patients with essential hypertension gave a hyper-reactor response to cold. The blood-pressure response to cold in patients with chronic nephritis was similar to that of normal subjects who were not hyper-reactors. A hyper-reactor response in a patient with increased arterial pressure would therefore exclude the possibility of hypertension due to chronic renal disease, but the converse is not true.

Clinical Estimation of Blood-Pressure

Palpation of brachial artery—H. N. Segall described a method of measuring the diastolic and systolic blood-pressures by palpation of arterial vibrations over the brachial artery. This is a modification of the auscultatory or auditory method described by Korotkow in 1905, and now in almost universal practice. The sphygmomanometer cuff having been inflated, the thumb is placed over the artery in the ante-cubital fossa at such a pressure that a faint sharp sensation, which is definitely not a pulsation, is felt. If the pressure of the thumb is too great, the pulsation of the artery is felt too strongly and tends to mask this other sensation. On allowing the air to escape, the familiar vibrations which the ear detects as sounds when the stethoscope is used, can be felt. The sharp change in amplitude at the transition from the fourth phase (loud sounds) to the fifth phase (faint sounds or disappearance of sounds) is somewhat more striking with vibration sense as the receptor. This method is particularly valuable for those with impaired hearing, or in cases in which a stethoscope is not available.

Treatment

Crataegus oxyacantha—J. D. P. Graham employed tincture of *Crataegus oxyacantha* in 10 cases of hypertension. Crude extracts of hawthorn had been employed in cardiac disease, hypertension, and morbid conditions of the chest since the Middle Ages. Investigations into the pharmacology of this herb showed that intravenous infusion of dilutions of the tincture, freed from alcohol, increased the gastric motility in anaesthetized guinea-pigs. The motor gradient of the isolated bowel of rabbits was reversed. In mammals intravenous infusion of similar dilutions of the tincture led to slowing of the heart-beat, prolongation of diastole with a tendency to idio-ventricular rhythm, and heart-block. The vagal centre in the medulla is stimulated, the early effects on the heart being inhibited by atropine. The isolated mammalian heart exhibits interference with the conducting system, while the avian heart reacts in a similar way. The coronary arteries of the sheep and rabbit and the pulmonary arteries and bronchi in the guinea-pig are constricted by crataegus. The carotid blood-pressure of cats anaesthetized with 0.5 g. of nembutal was depressed by 0.5 c.cm. of non-alcoholic tincture of crataegus per kilogram of weight. This effect was unaltered by atropinization of the animal. Subcutaneous injection of the tincture of crataegus had an antidiuretic effect on rats. The tincture was toxic to the liver of mammals if repeatedly administered subcutaneously, but did not induce morphological changes in the heart.

A large volume of the tincture of *Crataegus oxyacantha* was made by macerating 2 kg. of dry powdered whole fruits of hawthorn with 5 litres of 70 per cent alcohol for 7 days, with occasional stirring, filtering, pressing the marc, and mixing the fluids. This was assayed against international standard (1926) tincture of digitalis prepared from samples of leaf provided by the National Institute for Medical Research, Hampstead, London. The tincture of *crataegus* had a potency of 14.5 per cent of standard (1926) tincture of digitalis. The tincture is unpleasant to take in large quantities, but does not cause vomiting.

In 2 cases of auricular fibrillation and 2 of mitral stenosis with orthopnoea, oedema, and tachycardia, massive doses of the tincture were employed. Half an ounce was administered six-hourly up to a total amount of 20 ounces in 10 days. There was no improvement in the cardiac condition, and oedema advanced steadily. The drug was therefore abandoned as a competitor of digitalis. It was then tried in 10 cases of hypertension, some due to arteriosclerosis and some due to chronic nephritis. All had old-standing hemiplegic lesions, and several suffered from mild dementia. One fluid drachm of tincture of *crataegus* was given by mouth, three times daily in water. The daily readings of the blood-pressure were charted, and the drug was discontinued when it was felt that the pressure had been reduced enough. No ill-effects were complained of by any of the patients as a result of this administration. In every case the systolic and diastolic pressures were reduced 14 days after stopping medication. No other treatment was given, the patients being at rest in bed on a light diet. The average decrease in the systolic pressure was 54.5, and in the diastolic 28.5.

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Low Blood-Pressure

Postural Hypotension Causing Transient Paralysis

H. M. Thomas reported a case of recurring transient paralysis of the right arm and leg, the attacks occurring when the patient was in the upright position, and often soon after rising from a sitting or lying position. On examination it was found that he had a moderate form of postural hypotension which, in conjunction with cerebral arteriosclerosis, appeared to supply an explanation for the mechanism of the attacks. When elevated on a tilting table from the supine position to 75° erect posture, systolic blood-pressure fell below 90 mm. Hg, and temporary paralysis of the right leg occurred. This paralysis passed off in from 5 to 10 minutes, and, in the author's view, was due to a transient localized cerebral ischaemia occurring in the course of a fall in blood-pressure from postural hypotension. In some of the attacks momentary clouding of the vision of one eye occurred, this was probably due to temporarily inadequate blood flow through the ophthalmic branch of the internal carotid artery, or the central retinal artery.

Thomas, H. M. (1939) *Johns Hopk. Hosp. Bull.*, **65**, 329.

BLOOD TRANSFUSION

See also B.E.M.P., Vol. II, p. 530; Cumulative Supplement, Key No. 172; Surveys and Abstracts 1939, p. 250; and p. 34 of this volume.

Technique of Transfusions

Dried Blood-Plasma

F. R. Edwards *et al.* described the preparation and use of dried blood-plasma for transfusion. For many purposes for which blood transfusion is given, it is the plasma element that produces the desired effect; the red cells play a secondary

part. The chief constituents of plasma are the plasma proteins, and it is the administration of these, combined with fluids, which appears to be responsible for the resuscitative action in wound shock, post-operative shock, and burns. Further advantages are that plasma will keep indefinitely as compared with stored blood, which has a useful life of 14 to 28 days only, and that for the administration of plasma no grouping of the recipient is necessary. The ideal plasma for use is Group AB (I) plasma, but the plasma of any group may be given to any patient up to 500 c.cm. Group AB (I) plasma can be given in any amount. Group AB (I) plasma may be prepared artificially by mixing Group A (II) and Group B (III) bloods and withdrawing the resultant plasma. The dried plasma may be carried in ampoules and given by any intravenous saline apparatus. It can be stored at room temperature and will apparently remain effective indefinitely. Twenty grams of dried plasma dissolved in 250 c.cm. of distilled water or 500 c.cm. of 5 per cent glucose in distilled water is equivalent in plasma protein to 1 pint of citrated blood. The anti-shock property of dried blood appears to be comparable to that of whole blood. It is very useful in emergency, when no supply of whole blood is easily available, and in war surgery.

Human Serum as Blood Substitute

S. O. Levinson *et al.* state that human serum is an effective blood substitute for combating all the effects of severe haemorrhage, and resulting secondary shock, except the loss of red blood-cells. The loss of red blood-cells is not serious unless it is very extensive. Immediate restoration of fluid volume following extensive haemorrhage prevents the development of secondary shock. The best restorative agent, which is whole blood, requires time-consuming laboratory tests before administration, thus necessitating delay which counteracts its ultimate beneficial effects. Serum may be given in massive amounts without delay or preliminary testing, and can be used as an interval measure before blood transfusions or as a substitute measure when blood is not available or when loss of red blood-cells is not too extensive. Human serum as a blood substitute therefore should serve a wide use, not only in civil emergencies, but especially in wartime field injuries.

Haemoglobin Solution as Blood Substitute

L. O'Shaughnessy *et al.* discussed the use of a 5 per cent haemoglobin Ringier's solution as an intravenous substitute for blood. The solution can be stored longer than blood. It is important to keep the urine alkaline during the treatment. It was concluded that although efficient and safe the solution cannot be regarded as a complete substitute for blood. Four cases of anaemia from various causes were reported in which the solution was given with favourable results. Two of the patients developed rigors after the transfusion and some of them suffered from dyspnoea and discomfort. In one case the urine was inadvertently allowed to become acid and casts appeared in the patient's urine. In the other cases the urine was haemoglobin-free and in one case investigated the blood-plasma also contained no free haemoglobin.

Preserved Blood

J. C. Leedham-Green describes his experience of 60 transfusions from stored blood, one of the advantages of which, previously unrecorded, is that the *Treponema pallidum* dies after 20 hours in an ice-chest and therefore the danger of transmitting syphilis is diminished. There is not any need for complicated and expensive apparatus, the essentials are that the blood should be withdrawn under strict aseptic precautions into a closed bottle and stored on an average of 5.5 days at about 4° C. before use; one transfusion was given after 28 days' storage without untoward reaction. Fifty-three donors were bled to an average of 600 c.cm. from each donor, all of Group II or IV (Moss).

In 12 cases there were reactions, one with severe rigors, 8 with slight rigors, and 3 with fever, it is not improbable that other factors besides the blood may have been responsible in 4 of these cases. Slight haemolysis does not contra-indicate the use of the blood, but if the supernatant plasma has turned red it should be discarded.

Method of preservation—M. Maizels and N. Whittaker (1939) discussed the

preservation of stored blood. They found that the usual solutions in which blood is stored, such as the sodium chloride and citrate mixture of Harington and Miles, are hypertonic and therefore the erythrocytes tend to be destroyed. The authors showed by experiment that when starch or, even more effectively, dextrin is added to the citrate-saline solution, there is much less haemolysis. Blood has been kept in good condition for up to 7 weeks in this solution. The action of the polysaccharide in this capacity is not known. The following solution was recommended as isotonic for the storage of blood: sodium chloride 0.43 per cent, sodium citrate 1.05 per cent, and dextrin 8.5 per cent. 180 c cm of this solution should be added to 360 c cm of blood.

Use of sulphanilamide.—M. Novak described a method of preserving stored blood with sulphanilamide. It is usual in the United States to preserve the blood with 0.35 g. of sodium citrate in physiological saline to every 100 c cm of blood, and to store it at a temperature of 4 to 6 °C. This preserves the blood for about 10 days or more. Novak found that about 5 per cent of such blood stored for 10 days had become grossly contaminated with various organisms. This contamination may occur when the blood is collected. He found that the blood could be kept sterile by adding 20 mg. of sulphanilamide to every 100 c cm, and suggested that the drug may be of value in preserving other biological substances.

Effects of preservatives.—F. X. Aylward *et al.* studied the effects of various preservatives on stored blood. The anticoagulants tested were anhydrous sodium citrate, heparin, and anhydrous sodium citrate with glucose. It was found that in the plasma of stored blood there was an immediate rise in potassium, an initial fall followed by a gradual rise in inorganic phosphate, and a delayed and gradual rise in haemoglobin. In blood stored with a minimum of dilution, citrate-glucose appeared to be definitely better than citrate alone, and both were better than heparin as anticoagulants in delaying haemolysis and in retarding the chemical changes in the cells leading to increased values for plasma inorganic phosphate. None of these anticoagulants prevented the diffusion of potassium into the plasma, but citrate-glucose showed a lower value for plasma potassium, over a long period, probably owing to the lower degree of haemolysis.

Effect of diluents.—M. Maizels and N. Whittaker (1940) discussed the effect of diluents upon blood stored for long periods, of more than a month. The standard citrate-saline solution is hypertonic, and haemolyses the red cells. The authors found that 0.43 per cent sodium chloride solution and 1.05 per cent sodium citrate solution, formed a more efficient anticoagulant mixture. The addition of some carbohydrate, such as dextrose, also reduced the haemolysis appreciably. A 1.0 to 3.0 per cent solution should be used. Because a pH of about 6.6 was found to decrease the haemolysis to about half, the sodium chloride in the solution may be increased to 0.5 per cent to render the mixture more acid.

Toxicity of blood with high plasma potassium.—I. L. DeGowin *et al.* (1940, b) investigated the toxicity of blood with a high plasma potassium when transfused into human beings. Because the concentration of potassium in the plasma is highest after 15 days' storage, blood stored for 2 weeks or more was used. Intravenous toxic doses of potassium affect the conducting mechanism of the heart, possibly stopping its action. Animal experiments have shown that the amount of toxic reactions depends a good deal on the rate of transfusion. If given rapidly, large quantities of potassium reach the heart at the same time, and a fatal result was produced in dogs. Fourteen patients were transfused and it was found that, even if the blood had been stored for 30 days, no toxicity resulted if it were given at the rate of less than 43 c cm per minute. Blood taken from the recipient showed no significant increase in the value of the serum potassium.

Diffusion of potassium from erythrocytes.—Because potassium salts injected intravenously are toxic, I. L. DeGowin *et al.* (1940, c) investigated the diffusion of potassium salts from the cells to the plasma in stored blood. The investigated blood was stored at 3 to 5 °C and various preserving fluids were used. The amount of haemolysis was determined to see if the potassium was released by this means. The effects of temperature and the amount of carbon dioxide present on the diffusion of the potassium were also noted. It was found that none of these factors had any effect upon the diffusion, and that the amount of potassium in the plasma could not be accounted for by its liberation from haemolysed red cells. The potassium diffused

rapidly into the plasma during the first 5 days of storage and reached a maximal concentration in 15 to 20 days.

Partition of potassium—C. B. B. Downman *et al.* report on the variations in the plasma potassium level in blood stored according to the current practice of the Medical Research Council's Blood Supply Depots. The plasma potassium concentration rose rapidly during the first week averaging 102 ± 17 mg. per 100 c.cm. at 7 days, or 5 to 10 times the initial level, but thereafter the rise was comparatively slow. The source of the potassium is the red cells from which it is liberated quite independently of haemolysis. The plasma potassium concentration rises much less rapidly at room temperature reaching only 44 ± 7 mg. per 100 c.cm. in 6 days. The rate of redistribution of the ion was not reduced by reduction of the volume of the diluent, absence of foreign salts, increase of oxygen tension, or storage at 38°C . There was not any clinical evidence that the amount of potassium likely to be available in the volume of blood generally used for transfusion would be enough to produce toxic symptoms. The absence of toxic symptoms in patients receiving large volumes of stored blood suggests that this repartition of potassium may be of minor clinical importance only.

Transfusion of cold blood—Because warming stored blood tends to promote haemolysis, L. I. DeGowin *et al.* (1940, c) experimented with the transfusion of cold blood. Ten patients were given transfusions of stored blood mixtures at temperatures of 15° to 25°C . It was given at a rate of 6.0 to 42.8 c.cm. per minute and no harmful effects were noted from its use. In 568 cases the blood has been used clinically without reheating and no untoward results have been produced. Other parenteral fluids were given at room temperature and in 1,076 administrations only 32 were associated with any reaction. These patients experienced chill and fever. The authors pointed out that not having to warm intravenous fluids prevents any changes occurring in them and makes administration easier.

Incidence and types of reaction—E. L. DeGowin and R. C. Hardin (1940, a) reported on the incidence and types of reaction observed in a series of 1,458 transfusions of blood stored from 1 to 38 days, and 146 transfusions of fresh blood. There were no types of reaction specially characteristic of preserved blood. The incidence of various types of reaction did not increase or decrease with the period of storage. For citrated blood a limit of 10 days of storage was found to be safe. Blood stored in a dextrose-citrate mixture was found to be safe for 30 days of storage.

Factors influencing haemolysis—E. L. DeGowin *et al.* (1940, d) studied the various factors influencing haemolysis in preserved human blood. They considered blood unfit for transfusion if the haemoglobin content was such that haemoglobinuria was produced by its use. In this investigation Wu's colorimetric test was used to determine the amount of free haemoglobin in the plasma. It was found to be accurate for so small a quantity as 1 mg. of haemoglobin in 100 c.cm. of plasma. Many preservative solutions were investigated and it was found that the addition of large amounts of isotonic dextrose solution prevents a good deal of haemolysis. The best mixture consisted of 10 volumes of blood, 13 volumes of 5.4 per cent aqueous solution of anhydrous dextrose, and 2 volumes of 3.2 per cent dihydric sodium citrate (sodium citrate B.P.C.) in water. Much less haemolysis occurred at 5°C . than at 20°C . and the exclusion of air from the receiving vessel also helped to prevent it. The preservative should be cooled to 5°C . before the blood is added and this should be done as quickly as possible. Trauma, induced by shaking, did not produce so much haemolysis when dextrose was added to the preserving fluid.

Storage of Transfusion Plasma

F. A. Knott and F. H. Koerner stated that in cases of shock in which the haemoglobin level is not lowered it is better to give transfusions of plasma rather than whole blood. Group O plasma can be stored for a long time; moreover it can be removed from whole blood that has been stored too long for safe usage and stored again for some time. Precautions must be taken in its use because, although it does not contain the agglutinogens A and B it does contain α and β , and quickly clumps the cells of groups AB, A, and B. Therefore, if the plasma is to be given to patients of any other group but O, the effect of a 1 in 50 dilution of the plasma on their cells should first be noted.

Interchangeability of Serum and Plasma

C. H. Best and D. Y. Solandt, as a result of further experimental work in which serum and plasma were used interchangeably, stated that the results obtained with each were identical. With regard to the provision of fluid and also of serum proteins, which by their osmotic pressure retain fluid in the blood stream or attract it from the tissues, there is no significant difference between the two. No serious reactions have been obtained from the use of either. The authors concluded that serum and plasma are physiologically and therapeutically identical, and may be used interchangeably.

Placental Blood

L. P. Filippov describes the transfusion of placental blood. Its amount depends upon the size of the placenta and varies from 20 to 160 c.cm. with an average of 70 to 80 c.cm. Bacteriological control showed that blood from some placentae contained Gram-positive cocci. This bacteriological finding could not be improved by an improvement in the technique of taking and storing the blood. Placental blood is not only a substitute for lost blood (ordinary blood transfusion), but is a very active stimulant due to its high content of oestrone, gonadotrophic hormone, adrenaline, and other hormones. Other authors (Saizew and Golant) used successfully placental blood in various forms of psychopathy. Placental blood injections are more effective than protein injections in parametritis, cholecystitis, appendicitis and various inflammatory infiltrations. They also have a haemostatic effect and should be tried in cases of traumatic shock. No severe by-effects could be observed.

4 Drip Flow-Meter

S. R. Gloyne and P. M. Tooke Kerridge described a method of converting the blood transfusion equipment supplied to the London and Home Counties Emergency Blood Transfusion Service into a drip flow-meter (see Fig. 8). The transfusion may be started with a small amount of saline solution followed by blood at the rate of about 50 drops a minute. By this method the rate can be controlled and the amount easily measured. Two of the standard bottles and tubes are inverted, one containing citrated blood and glass beads and the other a sterile citrate-saline solution. The long glass tubes are closed by rubber-tubing and a glass plug to prevent any of the fluid entering the tube when the apparatus is being assembled. The short glass tubes are attached to a simple double-drip flow-meter provided with an air entry and a drain. If the blood level rises during a long transfusion and obscures the drop it can then be lowered by admitting air or draining some of the blood off. The air entry is at the uppermost part of the vessel to prevent air getting into the drip tubes or making a froth as sometimes happens when it is laterally placed. The

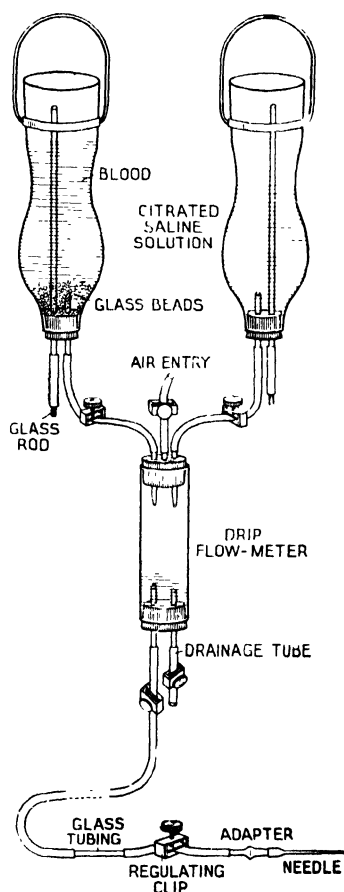


Fig. 8 Diagram showing blood transfusion equipment assembled as a drip flow-meter. (From *Lancet*, 1939.)

drip flow-meter is inserted about 6 inches below the level of the bottles, so that the whole apparatus hangs vertically and the level of the fluids in the bottles and the rate of dripping can be seen at a glance. From the flow-meter goes a rubber tube containing a glass section so that it is possible to see when fluid has reached the end of the tube and if any bubbles are present. From the tube a metal adapter goes to the needle so that it can be fitted on to the rubber without jerking the needle out of the vein.

Use of Whole Blood in Acute Infections

A. P. Krueger and M. J. Fuendeling stated that in staphylococcal infection it is necessary to combat both invasion by the organism and the toxin which it produces. If the individual is unable to do this, convalescent blood may supply the antibodies, or blood from an immunized donor may be used. Donors are given periodic injections of undenatured bacterial antigens to maintain a high level of immunity. Twenty c. cm. of their blood is given to the patient every 24 hours intramuscularly, or every 12 hours if the condition is very serious. The authors reported a case of extensive impetigo, one of acute mastoiditis, another of streptococcal parotitis, and a fourth of severe kidney infection following an operation for infected hydro-nephrosis treated by this method. In all cases the results were good and the patients recovered.

In Treatment of Haemorrhage

H. J. Brennan stated that during severe haemorrhage many of the patient's corpuscles get side-tracked, probably into muscle tissue. Fluid is also poured into the blood stream from the tissues, diluting the remaining corpuscles. This fluid is of lower osmotic pressure than plasma and the corpuscles therefore swell and cannot pass through the peripheral capillaries. Brennan concluded that it is not necessary to give whole blood to the patient, but a transfusion of plasma to return these corpuscles to the circulation again. This method, which has been previously used successfully for shock, has the advantage that it is unnecessary to group the patient and that no elaborate methods are needed for the storage of the plasma. Brennan treated 21 cases of haemorrhage successfully by this method, and suggested that the treatment should be used as a routine.

Volume and Rate in Treating Anaemia

H. I. Marriott and A. Kekwick discussed the importance of the volume and rate in blood transfusion for the relief of anaemia. They found that the volume of blood given depended upon the amount it was required to raise the haemoglobin level. If a rise of more than 33 per cent is required the transfusion should be divided, the 2 lots of blood being given at 2 days' interval. The amount needed depends upon the patient's size and can be calculated as follows:

$$\frac{\% \text{ rise of Hb required}}{100} \times \text{Patient's normal blood volume in c. cm.} \\ = \text{the amount required to raise the haemoglobin to the required percentage}$$

The rate of transfusion should never exceed 1 c. cm. per pound of body weight per hour. If the anaemia is so severe that the haemoglobin is less than 25 per cent, only 0.5 c. cm. per pound of body weight per hour should be given. If any signs of cardiac failure appear the transfusion should be stopped. This slow measured transfusion gives very much better results than the arbitrary method of giving any patient needing a transfusion a pint of blood in half an hour.

Malaria Conveyed by Subcutaneous Injection of Blood

Lesne *et al.* record the case of a male infant, aged 7 months, who had never been out of Paris, and when ill with broncho-pneumonia had daily intramuscular injections of the father's blood (5 injections of 10 c. cm. and 2 of 5 c. cm.) for a week. Two months later the infant had quartan fever which yielded to the administration of quinine, though the blood had not shown the presence of malarial parasites. Five weeks later and again 3 months later, when quinine treatment had been discontinued, the fever recurred, and on the second occasion malarial parasites

were recognized in the blood. It was found that the father, who appeared healthy, was born in the Cameroons and had had bouts of fever, but had been free from them for the 13 years since he had left that country. The authors regard this as the first case of accidental transmission by subcutaneous injection of blood from a malarial carrier. Reference is made to 3 cases of intravenous transfusion in which, from errors in technique, the donor was infected by a malarial recipient, and to 6 recorded cases in which unintentional malarial infection followed in the recipient of blood injected intravenously. The period of incubation after intravenous injection transfusion is said to vary considerably, but a mean of 8 days for tertian and of 30 days for quartan malaria may be regarded as probable.

Aylward, F. X., Mainwaring, B. A. S., and Wilkinson, J. I. (1940) *Lancet*, **1**, 685.

Best, C. H., and Solandt, D. Y. (1940) *Brit. med. J.*, **2**, 116.

Brannen, H. I. (1940) *Brit. med. J.*, **1**, 1047.

DeGowin, I. L., and Hardin, R. C. (1940, a) *Brit. med. J.*, **2**, 1.

- and Harris, J. F. (1940, b) *J. Amer. med. Ass.*, **114**, 858.

- and Swanson, L. W. (1940, c) *J. Amer. med. Ass.*, **114**, 859.

- Harris, J. F., and Plass, F. D. (1940, d) *J. Amer. med. Ass.*, **114**, 850.

(1940, e) *ibid.*, **114**, 855.

Downman, C. B. B., Oliver, J. O., and Young, I. M. (1940) *Brit. med. J.*, **1**, 559.

Edwards, F. R., Kay, J., and Davie, I. B. (1940) *Brit. med. J.*, **1**, 377.

Filipov, I. P. (1939) *Wien. med. Wschr.*, **89**, 1009.

Gloyne, S. R., and Kerridge, P. M. T. (1939) *Lancet*, **2**, 1267.

Harrington, C. R., and Miles, A. A. (1939) *Lancet*, **1**, 1348.

Knott, F. A., and Koerner, I. H. (1939) *Lancet*, **2**, 1069.

Krueger, A. I., and Luendeling, M. J. (1940) *Urol. cutan. Rev.*, **3**, 67.

Leadham-Green, J. C. (1939) *Brit. med. J.*, **2**, 849.

Lesne, Cayla, and Lichtenberger (1939) *Rev. du palud., Paris*, **1**, 92.

Levinson, S. O., Neuwelt, I., and Necheles, H. (1940) *J. Amer. med. Ass.*, **114**, 455.

Matzels, M., and Whittaker, N. (1939) *Lancet*, **2**, 1219.

(1940) *ibid.*, **1**, 590.

Marrion, H. I., and Kekwick, A. (1940) *Brit. med. J.*, **1**, 1043.

Novak, M. (1939) *J. Amer. med. Ass.*, **113**, 2227.

O'Shaughnessy, I., Mansell, H. I., and Slome, D. (1939) *Lancet*, **2**, 1068.

Wu, H. (1923) *J. Biochem., Tokyo*, **2**, 189.

BOILS AND CARBUNCLES

See also B. I. M. P., Vol. II, p. 547, and Cumulative Supplement, Key Nos. 173 and 174.

Boils

Treatment

Sulphamethythiazole.—C. G. Grulee and J. I. Mason employed sulphamethythiazole in 3 cases of furunculosis, particularly of the scalp, 2 in infants and 1 in a boy of 7. In one case the drug was given in doses of 0.5 g. every 4 hours. This dosage produced a blood level of about 8 mg. per 100 c.c.m. Within about 48 hours, old draining furuncles dried up almost completely, and for several days no new pustules appeared. This dosage was continued for 22 days, or until 66 g. had been administered. During this time only 5 new furuncles appeared. No ill-effects were noted. After a further short course the drug was discontinued, because of a sudden reduction in the percentage of polymorphonuclears. The dosage in the boy of 7 years was 1.0 g. every 4 hours. Six days after beginning treatment the scalp was entirely free of furuncles. In this case nausea and vomiting occurred, with a generalized morbilliform rash.

Grulee, C. G., and Mason, J. I. (1940) *J. Pediatr.*, **16**, 566.

BONE DISEASES

See also B. I. M. P., Vol. II, p. 553; and Surveys and Abstracts 1939, p. 253

Congenital Bone Dystrophies, Generalized*Dyschondroplasia*

T. Anwyl-Davies and F. Parkes Weber reported a case of dyschondroplasia (Ollier) of the upper limb with other developmental abnormalities. The dyschondroplasia affects the growing ends of long bones. It usually affects one extremity only. The normal ossification of the cartilage in the growing end of the affected bones does not take place. The condition is sometimes associated with multiple exostoses. The reported case occurred in a girl aged 10½ years. Her right arm was shortened and X-ray examination showed the lower end of the radius and the upper end of the humerus to end in thick nodular lumps. There were several 'chondromas' on the fingers and thumb. In addition, the child was mentally deficient. Her mother had received treatment for syphilis, but there was no evidence of the disease in the child. The patient also had a squint, fleshy eyelids, and epicanthus.

Anwyl-Davies, T., and Weber, F. P. (1940) *Brit. J. Child. Dis.*, **38**, 110

Congenital Hypoplasia of the Mandible

H. H. Weisengreen and F. D. Sorsky reported a case of congenital hypoplasia of the mandible, and pointed out that this condition must be recognized as a cause of cyanotic attacks in new-born infants. In this case respiratory difficulties were noted shortly after birth, and, in spite of tracheotomy of the tongue and supportive measures, the infant died 52 hours after birth.

Weisengreen, H. H., and Sorsky, F. D. (1940) *J. Pediat.*, **16**, 482

Fenestrae Parietales Symmetricae

Tj. Halbertsma records a family tree of 17 among whom the grandmother, not related to the grandfather, showed depressions over the areas usually affected by bony spaces in this abnormality. The grandparents had 6 children, 2 males showing the bony spaces, in the next generation 3 were affected, 2 females and 1 male. J. I. Lobstein, the elder, described the condition in 1772, and in 1937 R. Voigt collected 45 cases of this hereditary and familial condition. The openings in the parietal bones are close to each other on the crown of the skull and may be connected together by a narrow aperture. They are covered by skin under which the dura mater can be felt to pulsate as in the anterior fontanelle of infants. They vary in size from 0.5 to 4 or 5 cm. in length and 1 to 2 cm. in width. That on the right parietal bone is often somewhat larger than that on the left parietal.

Halbertsma, Tj. (1940) *Arch. Dis. Childh.*, **15**, 115

Lobstein, J. F., quoted by Voigt

Voigt, R. (1937) *Mscr. Kinderheilk.*, **70**, 224

Dysostosis Multiplex

J. B. Gillespie and I. A. Siegling report a case of dysostosis multiplex in a female infant, 16 months old. This syndrome, which is a subvariety of dyschondroplasia (multiple chondromas), is characterized by congenital clouding of the corneae, scaphocephalic head, kyphosis, limited extension of the joints of the extremities, dwarf stature, a combination of scaphocephalic and dyschondrotrophic deformities of the skull, dyschondrotrophic changes in other parts of the skeleton which give rise to shortness of neck and trunk, protrusion of the abdomen, kyphosis of the spine, partial ankylosis of the joints and other anomalies. In the case reported, X-ray examination of the chest showed very marked thickening of the ribs, due to subperiosteal new bone, and a marked clubbing of their sternal ends. There were dyschondrotrophic changes in the upper ends of the humeri and lower epiphyses of both bones of the forearm. The changes in the bones were regarded as evidence of florid rickets, and possibly of subclinical scurvy. The X-ray picture of cupping

of the long bones and the hazy moth-eaten appearance of the epiphyses would substantiate the diagnosis of rickets.

Gillespie, J. B., and Siegling, J. A. (1940) *J. Bone Jt Surg.*, **22**, 171.

Osteoporosis

Aetiology

Digestive tract disease—C. L. Brown *et al.*, in an investigation of 50 cases of generalized osteoporosis, found that 22 exhibited gastro-intestinal symptoms, 18 of these were females and 4 males. Among them the most common organic digestive disorder was chronic cholecystitis. Some cases were unquestionably examples of senile osteoporosis, but an examination of 6 typical cases below the age of 60, which revealed no organic gastro-intestinal lesion, furnished a clinical history of anorexia, abdominal distension with vague pains, nausea with, rarely, vomiting, eructations, and constipation. In the opinion of the authors, these symptoms were not due to osteoporosis, but probably to a calcium deficiency resulting in a chronic negative mineral balance. When blood serum-calcium and phosphorus determinations were made in 10 cases in the presence of gastro-intestinal symptoms, normal values were shown.

Brown, C. L., Vogel, S. R., and Meader, R. P. (1939) *Amer. J. digest. Dis.*, **6**, 628.

Leontiasis Ossea

Ophthalmological Complications

According to S. Philps leontiasis ossea may be due to creeping periostitis of the bones of the face and skull or diffuse osteitis of these bones. The latter condition may be general, circumscribed, or local. He reported a case of circumscribed osteitis of many years' standing in a man of 33 years, the left parieto-occipital area and the left frontal bone were affected. The left orbit was displaced downwards and the left eye was 15 degrees convergent. The visual field and visual acuity were normal and there was no proptosis. Linear osteotomy of the left parietal area was performed to relieve headache, and pathological examination showed osteitis fibrosa. Two months later, however, he knocked his head, the swelling of the head increased, and the headaches returned, though not so severely.

Philps, S. (1939) *Brit. J. Ophthalm.*, **23**, 729.

Osteitis Deformans

Pathogenesis

According to D. R. Nichols the pathological process in osteitis deformans is a transformation of the vascular elements of the Haversian canals and bone marrow into hyperplastic connective tissue which invades the cortex of bone and enlarges the Haversian canals. New bone is then deposited on this connective tissue in an irregular manner, resulting in thickening of the cortex of the bone and narrowing of the medullary cavity. The causation is unknown. The symptoms vary, pain may be absent, the head and long bones are chiefly affected, and foramina in the skull and spine may be narrowed and pressure exerted on nerves. Serum phosphatase is nearly always much raised, occasionally by 40 times the maximal normal amount, and this is often proportional to the extent and activity of the bone changes. No known treatment alters the course of the disease, but pain can sometimes be relieved by orthopaedic or neuro-surgical procedures.

Treatment

Adrenal cortical preparations—L. M. Watson reports some benefit, especially relief of pain, in osteitis deformans from injections of cortin (extract of adrenal cortex) into the gluteal muscles. The cause of osteitis deformans has not been decided, though several suggestions have been made, such as endocrine imbalance between the parathyroid and adrenal cortex, and disordered metabolism. The most striking evidence of metabolic disturbance is the greatly increased phosphatase activity of the blood serum, the calcium and phosphorus content of the serum remaining normal. Phosphatase, an enzyme capable of hydrolyzing phosphoric esters, such as glycerophosphates, is present normally in the blood and tissues,

but especially in actively growing bone and cartilage. Though increased in other diseases, it is most strikingly so in osteitis deformans, but it should be regarded as an effect rather than the cause of the disease. Walton, in 1928, found that fresh or dried whole adrenal gland by the mouth relieved the pain of characteristic osteitis deformans, but not of the form in which one bone only is affected. In 9 patients recorded by Watson cortin treatment, 5 to 10 c.cm. per week, was followed in all by a fall in the serum phosphatase, and in 6 there was subjective improvement, especially as regards pain. Injections of synthetic cortical hormone (desoxycorticosterone acetate) and desiccated adrenal cortical extract were not so effective as cortin. Long continued administration of cortin to persons without cortical hypofunction might possibly cause atrophy of the adrenal cortex. The author does not consider that osteitis deformans is a manifestation of adrenal insufficiency, but he suggests that cortin may in some peculiar way influence the underlying metabolic derangement in osteitis deformans, and points out that, at present, treatment by cortin is at the best empirical.

Nichols, D. R. (1940) *Proc. Mayo Clin.*, **15**, 182.

Walton, A. J. (1928) *Textbook of Surgical Diagnosis*, Vol. I, p. 330.

Watson, I. M. (1939) *Canad. med. Ass. J.*, **41**, 561.

Acute Osteomyelitis

Recurrent Infection

Toxoid treatment—I. C. O. Valentine and L. C. B. Butler stated that recurrent foci, which may form abscesses, occur in staphylococcal osteomyelitis. They may form in the site of an old sinus, in soft tissues, or in bone. They are sometimes seen after infected war wounds, and lead to chronic ill-health. The authors treated 30 such cases with toxoid and obtained encouraging results. Injections were given over a number of years to maintain a constant level of immunity. Because antitoxins may be higher in the pus than in the serum of these patients, it is important to use a toxoid containing a potent leucocidal and only a moderate haemolytic factor. It is possible that the treatment may activate a latent focus.

Valentine, F. C. O., and Butler, L. C. B. (1940) *Lancet*, **1**, 914.

Tuberculosis

Of Mandible

C. M. Meng reports 14 cases of tuberculosis of the mandible, a condition hitherto considered to be rare. Eight of these cases were seen within a period of 2½ years. In most cases patients were in the second and third decades of life. The chief manifestations were swelling, discharging sinuses, and occasionally trismus of the jaw. In about 43 per cent of the cases there were tuberculous bone lesions elsewhere, and in 29 per cent the skull was affected. Of 10 cases, in which the chest was examined by X-rays, there was evidence of tuberculosis of the lungs in 8 and of the pleurae in 2. The author considered that tuberculosis of the mandible is almost always haematogenous, arising from a primary focus which is generally in the lungs. In some cases, however, the mandible may be involved by extension of a tuberculous process from the mucous membrane of the mouth, or from infected gums around carious teeth.

Treatment

Insulin.—R. L. Nichols and E. L. Compere stated that the successful management of cases of bone and joint tuberculosis depends upon improvement in the nutrition and general health of the patient. Fourteen such patients were given 2 to 5 units of insulin 20 minutes before each meal in an attempt to stimulate their appetites. All the patients showed greater interest in their food. Their general health and well-being improved and a gain in weight was noted. Two of the children who had been unsatisfactory before the treatment continued to gain weight even after it was stopped. The effect of the insulin was attributed to improved appetite, absorption, and assimilation of food.

Meng, C. M. (1940) *J. Bone Jt Surg.*, **22**, 17.

Nichols, R. L., and Compere, E. L. (1939) *J. Bone Jt Surg.*, **21**, 885.

Tumours of Bone

Malignant

Multiple myeloma—H. Ulrich reported a case of multiple myeloma with weakness as the most prominent symptom. Testicular tumours developed and there was albuminuria, but no Bence Jones proteose. The blood showed a severe anaemia and myelocytes, myeloblasts, and 'plasma cells' were present in the circulating blood. X-ray examination showed no definite evidence of bone disease, though films taken of the skull after necropsy showed a few small punched-out areas. Negative Aschheim-Zondek tests excluded teratoma. The left testicle was removed for examination and showed several small tumours, made up of atypical plasma cells and young myeloid cells. The patient became weaker, developed haemorrhages, and died in spite of 5 blood transfusions. Post-mortem, the spleen, kidneys, testis, and bone marrow were infiltrated with abnormal atypical plasma cells. A diagnosis of multiple myeloma of the so-called plasma-cell type was therefore made.

From a review of the literature, the author concluded that multiple myeloma is a neoplastic disease midway between the frank tumours and the leukaemias. The cells of the growths are of myeloid origin usually resembling plasma cells. Although the usual site of origin is the bone marrow, it may be extramedullary. The outstanding symptoms are weakness and pain, the latter often only after injury to diseased bone. It should be thought of in a case of unexplained backache. Renal involvement is common, sometimes as a hydronephrosis secondary to tubular obstruction by casts of Bence Jones protein. Occasionally removal of a solitary tumour or X-ray therapy produces a cure. As a rule, the prognosis is hopeless, though X-rays may relieve pain. In diagnosis the following are of value: (i) X-rays—though it may be impossible to differentiate a myeloma from a metastatic carcinoma, (ii) biopsy of the involved bone, (iii) sternal puncture, (iv) hyperproteinaemia of about 10 per cent, (v) hypercalcaemia, with a normal serum phosphorus, (vi) Bence Jones proteinaemia which may be absent, (vii) myeloma or 'atypical plasma cells' in the circulating blood. These are rare but diagnostic.

M. Jersild stated that the blood serum in myelomatosis differed from normal serum in many ways. Thus the protein is increased mainly in the globulin fraction and this is shown by increased serum lability which may be shown in many different ways. It is therefore possible to diagnose the disease by investigation of the serum. After the serum of myelomatosis patients has been heated to about 60°C it is able to fix complement. The complement-fixation test was positive in 13 of 27 patients and 5 more probably had myelomatosis. Increase in globulin was also found and the coagulation temperature of the serum was often low. Jersild stated that if complement was fixed but there were no changes in the serum protein the diagnosis of myelomatosis was uncertain.

Carcinomatosis—A. M. G. Campbell reported 7 cases of carcinomatosis of bone which were originally diagnosed as chronic rheumatism. The correct diagnosis depends upon the character of pain, the blood-picture, and the X-ray findings. The pain is deep-seated and gnawing in character. It is not relieved by ordinary analgesics or by local applications nor is it affected by movement. The blood-picture may be normal or merely show a hypochromic anaemia. Should it show a leuco-erythroblastic anaemia this is very valuable in diagnosis. Radiographic findings are diagnostic but are often not present till late. Pathological fracture may occur and other general signs of metastases may be present to help in diagnosis.

Osteogenic sarcoma—A. B. Ferguson, reviewing 400 cases of osteogenic sarcoma of which 258 were treated by amputation, found that only 8 per cent survived early amputation. Those who consider that early amputation is a proper treatment for osteogenic sarcoma of an extremity doubtless expect that the earlier the amputation, the better is the result. This is not the case. With amputation in the first month after the earliest evidence of symptoms none of 13 patients survived; with amputation in the second month 1 of 25 survived, in the third month 2 of 23 survived, in the fourth, fifth, and sixth months 8 of 73 survived. There is not any rational explanation for this. The following lines of treatment are recommended for osteogenic sarcoma of an extremity: (i) avoidance of early amputation, (ii) delay of amputation, (iii) radiation before amputation, (iv) radiation, excision, and

implantation of a bone graft or bone chips before amputation, with amputation following before recurrence becomes evident; and (v) repetition of excision before amputation, if recurrence is evident before amputation has been carried out

Subperiosteal Giant-Cell Tumour of Mandible

W J Potts reported a case of subperiosteal giant-cell tumour of the mandible in a male, aged 16. Geschickter and Copeland (1931) stated that giant-cell tumours arise only in bone which is preformed in cartilage. They predicted that, since the periosteum has osteoclastic properties, any giant-cell tumour arising from bone preformed in membrane should be subperiosteal. This case appeared to confirm this hypothesis.

Xanthoma

S. Drăganescu and S. Tzovaru described a case of generalized bony xanthomatosis in a boy aged 16. He complained of marked disability, with flexion contractures of the limbs, and pain on movement. Radiography of the shoulders, knees, and hips showed rarefied areas in the bone. There were also some fluctuating swellings, which on aspiration showed crystals of cholesterol material in the fluid. Biopsy revealed reticulo-endothelial cells filled with vacuoles. The condition, which is rare, differs from Schuller-Christian disease in that there is no involvement of the cranium, no exophthalmos, and no diabetes insipidus.

Campbell, A. M. G. (1940) *Lancet*, **1**, 777

Drăganescu, S., and Tzovaru, S. (1939) *Rev. Chir., Paris*, **58**, 448

Ferguson, A. B. (1940) *J. Bone Jt. Surg.*, **22**, 92

Geschickter, C. F., and Copeland, M. M. (1931) *Amer. J. Cancer*, **15**, 524.

Jersild, M. (1939) *J. Amer. med. Ass.*, **113**, 1119

Ulrich, H. (1939) *Arch. intern. Med.*, **64**, 994

Potts, W. J. (1940) *J. Bone Jt. Surg.*, **22**, 417

BRAIN: REGIONAL DIAGNOSIS

See also B. I. M. P., Vol. II, p. 609, Surveys and Abstracts 1939, pp. 94 and 255, and pp. 64 and 71 of this volume.

Lesions of Frontal Lobe

Effect of Right Frontal Lobectomy on Intelligence and Temperament

I. Lidz studied the intellectual functions and personality traits in a man of high intelligence before and after removal of his right prefrontal region on account of a tumour. The section bordered upon the anterior portion of area 6 of Brodman. The only resulting physical sign was slight increase in the deep reflexes of the left extremities. Tests selected to estimate intelligence and alterations in temperament, and careful observation of the patient's behaviour, were negative; there was no deterioration in ability for abstract work, and the results of the tests coincided with the impressions of the patient and of those who were able to observe him carefully.

Effect of Removal of the Frontal Poles in Rats

Experiments have previously been performed on monkeys to find out the part played by the frontal lobes in the regulation and control of spontaneous activity. It was demonstrated that the cortex plays an important part in the production of increased activity. But it was not demonstrated whether the lesions simply made inactive animals more active or normally active animals abnormally active. Furthermore there was no way of evaluating the changes in behaviour and metabolism which accompany the increase of activity. C. P. Richter and C. D. Hawkes experimented on rats; 2 groups of animals were selected, the animals in one of which were much less active than the normal average and those of the other much more active than the normal average.

The result was as follows. (i) By means of activity-drums and cyclometers, quantitative study was made of the effects produced on spontaneous activity of rats by removal of the frontal poles of the brain (the cortex and the tip of the

corpus striatum), (ii) both unilateral as well as bilateral lesions increased activity greatly. Removal of both poles produced a condition of definite hyperactivity, i.e., the rats reached activity levels never attained by normals, (iii) these lesions increased food intake, decreased body weight, but had no effect on water intake, (iv) at necropsy the ovaries weighed more and the pituitaries less than those of control animals of the same age, and (v) since the animals became very distracted, irritable, and savage when thwarted, it was concluded that the picture presented greatly resembled that of manic conditions seen in humans.

Idz, T. (1939) *J. Neurol. Psychiat.*, N.S. **2**, 211.

Richter, C. P., and Hawkes, C. D. (1939) *J. Neurol. Psychiat.* N.S. **2**, 231.

Lesions of Temporal Lobe

H. S. Sanford and H. L. Bau report on the 292 cases which have, up to 1937, been diagnosed 'tumour of the temporal lobe' in the Mayo Clinic. In 211 of these cases the presence of a tumour was proved at operation, at necropsy, or by removal of typical glomatous cystic fluid. From examination of these 211 cases the following conclusions were drawn: (i) Homonymous hemianopia is the commonest visual field defect produced by tumours of the temporal and occipital lobes. (ii) Quadrantic anopias are produced more frequently by tumours of the temporal lobe. (iii) Normal fields occur with approximately the same frequency in cases of tumour of the temporal and occipital lobe. (iv) Sparing of the macula occurs more often in tumours of the occipital lobe. (v) There was forward looping of the geniculocalcarine fasciculus, described by Meyer, lesions of this portion of the fasciculus may produce a typical picture. (vi) Incongruous homonymous field defects were produced by tumours of the temporal lobe, affecting either the lateral aspect of the homolateral optic tract or the beginning of the geniculocalcarine fasciculus. In the former case the larger defect is in the field of the homolateral eye; in the latter, in the field of the contralateral eye. (vii) No concrete evidence was obtained either for or against the presence of a crossing bundle of fibres to allow representation of each half of the retinal macula in both occipital lobes. (viii) The presence or absence of choked disks and the equality or inequality of the degree of choking in the two eyes are of no clinical value in deciding on which side of the brain a tumour of the temporal lobe is situated. Although with unequal degrees of choking of the disks in the two eyes it is more probable that the tumour will be on the same side as that on which the choked disk is most severe, this criterion is not sufficiently reliable to be of any value in lateralization of the tumour. (ix) Visual disturbances other than the field defects are of no value to help in the diagnosis or lateralization of tumours in the temporal lobe.

Sanford, H. S., and Bau, H. L. (1939) *Arch. Neurol. Psychiat., Chicago*, **42**, 21.

BRAIN TUMOUR

See also B. I. M. P., Vol. II, p. 619, and Surveys and Abstracts 1939, pp. 94 and 257.

Tumours of Medulla, Pons, and Mid-brain

O. Foerster *et al.* made a microscopical examination of 21 tumours of the medulla oblongata, pons, and mid-brain. In 13 other cases they observed a tumour at operation, but it was impossible to examine them histologically. Four other cases not examined during lifetime by the authors of this paper were also examined microscopically. Histological examination showed the following types of tumour: astrocytoma, 12; spongioblastoma polare, 1; gangliocytoma and ganglioglioma, 3; medulloblastoma, 1; glioblastoma malignum, 7, and metastases of carcinoma, 1 case. A detailed report is given of the signs observed in these cases. With regard to treatment, it is noteworthy that the authors recommended an operation for all these cases, provided the patient's general health did not contra-indicate it, although the therapeutic value consisted only in reduction of pressure.

Foerster, O., Gagel, O., and Mahoney, W. (1939) *Arch. Psychiat. Nervenheilk.*, **110**, 1.

Tumours of Corpus Callosum

Brouwer and, later on, Michelsen reported a syndrome believed to be characteristic of a tumour of the corpus callosum. They observed intense psychic disturbance, fever not explained by any affection, pleocytosis in cerebrospinal fluid, increased albumen and xanthochromia. The value of this syndrome for diagnosis of tumours of the corpus callosum was confirmed by K. W. Essen who examined two cases on which later necropsy was performed. Signs of apraxia in the left hand were not observed.

Essen, K. W. (1939) *Nervena-t* **12**, 405

Metastatic Tumour:

Intracranial Metastasis of Carcinoma

According to W. Scheid about 20 per cent of intracranial tumours probably result from metastasis. Primary carcinoma of the bronchi has been frequently demonstrated. Metastasis takes place either into brain membranes or into brain substance. Metastasis into the dura mater gives the symptoms of pachymeningitis haemorrhagica. Metastasis into the pia mater produces the signs of meningeal irritation (stiff-neck, epileptiform attacks, psychical abnormality and defective function of the cranial and spinal nerves). Tumour cells may be observed in the cerebrospinal fluid which contains much albumin. The order of appearance of the clinical symptoms varies; the illness lasts one week only in some cases, in other cases several months. Metastasis into the brain substance is much more frequent. In some cases violent headache occurs in spite of only poor signs demonstrated at examination; there is no typical symptomatology. Increased pressure had been observed only rarely, probably in consequence of extensive destruction of the brain substance. Often few clinical symptoms only are observed; extensive destruction, however, of the brain substance has been observed at necropsy. In these cases the symptoms of the primary tumour remain in the background.

Scheid, W. (1939) *Mitg. Z. Psychiat.* **113**, 66

Tuberculomas

H. F. Buchstein and A. W. Adson stated that tuberculomas of the brain occur at all ages, and, with few exceptions, arise by haematogenous metastasis from a tuberculous focus elsewhere, generally in the lungs or related lymph nodes. Tuberculomas producing symptoms of tumour of the brain develop most frequently in adolescents and young adults with a single extra-cranial focus. Those associated with tuberculous meningitis tend to occur chiefly in children and in the presence of generalized tuberculosis. Laboratory studies do not aid in the differential diagnosis. Treatment must be directed against tuberculosis as a disease, as well as against the local lesion, if possible. Removal of cerebellar tuberculomas almost always ends in disaster. Fibro-calcous tuberculomas of the cerebrum, and arachnoid tuberculomas are the best subjects for surgical removal, and good results follow operation in a gratifying percentage of cases.

Buchstein, H. F., and Adson, A. W. (1940) *Arch. Neurol. Psychiat., Chicago*, **43**, 635

BREAST DISEASES

See also B.I.M.P., Vol. II, p. 657, Cumulative Supplement, Key Nos. 191-197; Surveys and Abstracts 1939, pp. 35, 109, and 260, and p. 21 of this volume.

Congenital Lesions

Supernumerary Breasts

Tibor de Cholnoky stated that supernumerary breasts may occur anywhere along the milk line if it does not disappear normally during development. The line extends from the axilla to the pubic region, ending at the inside of the thigh. Supernumerary breasts may, however, occur in atypical sites. Most observers consider the condition to be inherited. Aberrant breast tissue is nearly always found in the axilla, and in

the author's series all were women. Polythelia (multiple nipples) is relatively frequent, sometimes being confined to one breast. The author reported a case of a well-developed complete breast in the right Scarpa's triangle in a female. It enlarged during pregnancies, but did not secrete. Forster reported a case of pseudomamma in the same site in a man. The breasts must be distinguished from lipomas and other benign tumours. They do not usually cause symptoms unless they are in an awkward position, begin to function, or malignant or other tumour formation occurs in them. Surgical treatment is indicated only if these symptoms arise, or if the patient is worried by the condition.

de Cholnoky, T. (1939) *Arch. Surg., Chicago*, **39**, 926

Inflammations

Acute Mastitis of Lactation

Treatment—F. Guercio discussed the treatment of puerperal mastitis and mammary fistula. In many cases it is a considerable time before the abscess points or even develops and the lactation is therefore seriously disturbed. The author tried testosterone propionate in this condition and found that 0.01 g. injected daily up to a total of 0.25 or 0.3 g. stimulated abscess formation and pointing and at the same time relieved the diffuse tension caused by the inflammation. Large doses inhibited lactation and therefore are regarded as injudicious.

Chronic Mastitis

Testosterone propionate therapy—A. W. Spence treated 16 women with chronic mastitis with intramuscular injections of testosterone propionate in a dosage varying from 25 mg. to 100 mg., usually twice a week, for several months. Of these patients 12 had lumps in the breast. In 3 of them the lump disappeared, in 5 they were reduced in size, but in 2 fresh lumps appeared during the treatment. In 14 patients the pain in the breasts was relieved. Twenty-four control patients were given intramuscular injections of olive oil, and in 13 of them the pain was relieved. Testosterone propionate produced some degree of virilism in some of the patients. The growth of hair increased in 5 patients, menstruation was suppressed in 7, and in 1 receiving a large dose the clitoris was enlarged and the endometrium atrophied.

Guercio, F. (1939) *Arch. Soc. ital. Ostet. Ginec.*, **35**, 353.

Spence, A. W. (1939) *Lancet*, **2**, 820.

Malignant Tumours

Paget's Disease of the Nipple

In further observations, based on 42 cases, Robert Mun concluded that Paget's disease of the nipple and the carcinoma of the breast ordinarily associated with it are both secondary to an intraductal carcinoma of the mamma. An intraductal carcinoma is defined as an anaplastic malignant growth proliferating within a lactiferous duct, but not penetrating through its walls. The Paget cells are malignant cells which have spread from the ducts and grow 'intra-epidermically'. Two other views have been put forward as regards the relation between Paget's disease of the nipple and the carcinoma of the mamma: (i) that Paget's disease of the nipple causes the mammary carcinoma, and (ii) that the mammary carcinoma causes Paget's disease of the nipple.

Carcinoma

Aetiology. Endocrine dysfunction—W. Cramer investigated the possible hormonal aetiology of breast cancer. A high susceptibility to breast cancer in two strains of mice was associated with degeneration in the adrenal medulla. It could be diminished either by removing the supply of the adrenal cortical hormone, or by applying an excess of an anterior pituitary hormone. From this the author concluded that breast cancer is not a fixed and unalterable quality residing within the organism, but can be modified; it does not reside entirely, if at all, within the mamma; it is conditioned partly by a disturbance of the endocrine balance.

Mammary tumours produced in rats by oestrone.—R. L. Noble *et al.* review the experimental production, especially in mice, of mammary carcinoma by oestrone

and refer to C. F. Geschickter's report of carcinoma in rats after 23 days of oestrone treatment. Noble *et al* report their observations on mammary tumours produced in female rats from 5 to 7 days old by the implantation of pellets of crystallized oestrone subcutaneously. Mammary tumours composed of mammary tissue showed very active hyperplasia of epithelium, but not carcinomatous change in 28 out of 49 rats. The first tumour to become palpable was after 226 days of treatment. The tumours were often multiple and were not near the site of the implanted pellets. Other effects usually associated with prolonged oestrogen treatment, such as pituitary enlargement and adenomas, ovarian atrophy, uterine fibrosis with squamous-celled metaplasia, and alteration in bodily growth, were noted. A number of the rats were hypodermically injected with the pituitary thyrotrophic hormone, each rat receiving daily injections for 8 months after the implantation of the pellets, in order to study the protective or curative effect described by Cramer and Hoising, in 17 out of 25 animals thus injected, or 68 per cent, tumours appeared, whereas 11 out of 19 controls, or 58 per cent, showed tumours. This treatment obviously had not any influence on the incidence of the tumours.

Ingestion of oestrogen—H. Auchincloss and C. D. Haagensen reported a case of carcinoma of the breast in a woman of 47 who had previously received injections of oestradiol benzoate over a period of 2½ years—the total dosage being 79.067 mg.—to combat the symptoms of artificial menopause due to irradiation. The patient had a family predisposition to cancer, especially cancer of the breast. The authors had shown that in mice this hereditary factor is a prerequisite for the induction of breast cancer by oestrogenic substance. If this relationship between heredity and the effect of oestrogen holds good in human beings, as well as in mice, the authors inferred that their patient was one of those individuals in whom oestrogenic substance might have induced breast cancer. Although the authors could not conclude that oestradiol benzoate was definitely a contributing cause, they regarded it as quite possible, even probable, that it was. They felt that, until more is known of the action of oestrogenic substance, its use should be avoided in large doses when there is a family history of breast cancer, and in patients with chronic mastitis, carcinoma, or any breast neoplasm, either before or after surgical or irradiation therapy.

Prognosis—G. W. Taylor and N. H. Bruce analyse 319 cases of carcinoma of the breast in which radical mastectomy had been performed, and conclude that large lesions and those with skin involvement or extensive axillary involvement had a poor prognosis which in many cases, even in the absence of remote metastases, contra-indicated operation. Old age, obesity, and high blood-pressure increase the risk. Although a definite prognosis in any border-line case is still impossible, the authors consider that the chance of cure should be carefully weighed against the operative risk and the normal expectation of life, this might lead to palliative measures being employed more often than at present.

Treatment. Preoperative irradiation—H. H. Trout stated that preoperative irradiation of breast cancer is particularly indicated in patients having palpable nodules in the axilla, in cases in which growth is fixed either to the skin or to the underlying muscle, in rapidly advancing cases, in pregnancy, and in a few apparently inoperable cases. The author employs 15 to 20 small needles (3 to 5 mg. each) of radium, implanted under the skin in different localities at the time of operation. In women before the menopause, irradiation of the ovaries is particularly indicated if the tumour is growing rapidly, if there is an associated infection, or if pregnancy is present.

Intramammary squamous-celled carcinoma—S. W. Harrington and J. M. Miller report the case of a single woman, aged 54, who for 2 months had noticed a rapidly growing, moderately painful tumour in the right breast. A blood-stained discharge could be expressed from the nipple, a bluish cutaneous discoloration was present over the breast, and X-ray examination showed metastatic neoplastic destruction of the ninth rib. Wide-spread removal of the breast, followed by 3 courses of radiotherapy, were carried out, but recurrence proved fatal. The growth arose in the depth of the mamma and was quite distinct from carcinoma arising from the skin or the nipple. The authors refer to 5 previously reported examples of this rare form of mammary carcinoma (Ribbert, Hoell (2), Calderara, Delbet and Mendaro), and mention that cholesteatomas and simple dermoid cysts, in which malignant

change has been reported, are the commonest tumours in the depths of the breast to contain pavement epithelium. The occurrence of a squamous-celled carcinoma deep in the mamma could be explained either by Cohnheim's theory of displaced foetal cells or as a result of metaplasia.

Sarcoma

J. M. Miller and S. W. Harrington analyse 37 cases which include adenofibrosarcoma (24), 'pure' fibrosarcoma or spindle-celled sarcoma (9), lymphosarcoma, haemangio-endotheliosarcoma, and a mixed growth of sarcoma and carcinoma. Since it was recognized that the great majority of sarcomas of the breast arise in adenofibromas of the breast, the number of cases of 'pure' sarcomas reported has fallen off. The prognosis of these 2 groups is very different, being much better in the adenofibrosarcomas than in the pure fibrosarcomas. In addition to the above cases seen at the Mayo Clinic, the authors collected from published sources 7 cases of chloroma, 3 of lymphoid leukaemia, 5 of lymphogranuloma, and 4 of lymphosarcoma involving the mamma.

- Auchincloss, H., and Haagensen, C. D. (1940) *J. Amer. med. Ass.*, **114**, 1517.
 Calderara, A. (1910) *Vuchows Arch.*, **200**, 181.
 Cramer, W. (1940) *Amer. J. Cancer*, **38**, 463.
 and Horning, F. S. (1938) *Lancet*, **1**, 72.
 Delbet, P., and Mendaro, quoted by Pasterneck, J. G. and Wirth, J. I. (1936) *Amer. J. Path.*, **12**, 423.
 Geschickter, C. I. (1939) *Science*, **89**, 35.
 Harrington, S. W., and Miller, J. M. (1939) *Proc. Mayo Clin.*, **14**, 484.
 Miller, J. M., and Harrington, S. W. (1940) *Proc. Mayo Clin.*, **15**, 278.
 Muir, R. (1939) *J. Path. Bact.*, **49**, 299.
 Noble, R. I., McEuen, C. S., and Collip, J. B. (1940) *Canad. med. Ass. J.*, **42**, 41.
 Ribbert, H. (1904) *Geschwulstlehre für Ärzte und Studierende*. Bonn, p. 416.
 Taylor, G. W., and Bruce, N. H. (1940) *New Engl. J. Med.*, **222**, 790.
 Froell, A. (1908) *Nord. med. Ark.*, **1**, 1.
 Trout, H. H. (1940) *Ann. Surg.*, **111**, 700.

BRONCHIECTASIS, BRONCHIOLICTASIS AND BRONCHIAL SPIROCHETAL TOSIS

See also B. I. M. P., Vol. II, p. 682, Cumulative Supplement, Key Nos. 199-201 and Surveys and Abstracts 1939, pp. 114 and 265.

Bronchiectasis

Clinical Picture

X-ray appearances of cystic bronchiectasis - D. Reisner and I. G. Ichertkoff report on clinical and radiological examination of 17 patients with cystic bronchiectasis, which they regard as a distinct disease and separate from the common forms of saccular bronchiectasis and from other cystic changes in the lungs. Of the 17 patients, 12 were males, the ages ranged from 11 to 70. In a large proportion of the cases respiratory symptoms were absent or very mild, and often quite out of proportion to the prominent physical signs and to the X-ray appearances in the lungs. Five cases presented definite symptoms such as cough, with or without expectoration, which was never fetid. As a rule examination of the chest did not show visible deformity or retraction of the chest wall, the percussion note over the affected area varied, being either impaired, normal, or hyperresonant. The breath sounds were either bronchovesicular, bronchial, or sometimes diminished. There were generally numerous moist râles and many rhonchi. The characteristic X-ray findings were as follows: the involved portion of lung showed a honeycomb or sponge-like appearance, often giving the impression of a bizarre network composed of meshes of various sizes. This appearance was due to a cluster of thin-walled, closely-packed cavities, separated by fine trabeculae. The cavities were

generally round or ovoid, their size ranging from that of a pea to a walnut. Small fluid levels were often present at their lower poles. Fibrosis and shrinkage of the lung were generally absent, and in most cases there was not any alteration in the position or shape of the mediastinal structures or heart, narrowing of the intercostal spaces, or distortion of the contours of the thorax. Some cases, however, showed varying degrees of surrounding fibrosis and infiltration with resulting retraction of the pulmonary field.

Treatment

Sulphapyridine—M. F. Cordey describes 2 cases of bronchiectasis treated with sulphapyridine. The first patient was an adult who had suffered for 2 or 3 years from bronchial dilatation and subsequent bronchiectasis. He expectorated 150 c cm daily, this amount could be reduced by treatment with inhalations and various drugs to about 50 c cm. The author then tried sulphapyridine (M & B 693, dajenan) in a dosage of 6 tablets daily. After the third day there was only 20 c cm of sputum. It was found that a minimal dose of 2 tablets (1 g) daily kept the amount of sputum at a minimum. The second patient was a 6-year-old girl with severe bronchiectasis and producing 250 c cm of sputum daily. Sulphapyridine was given in a dose of 2 tablets daily for 1 week, followed by an interval of 1 week; the following week 2 tablets were given daily, and the fourth week 2 tablets every second day, then for 8 weeks 3 tablets per week. There was no further cough or sputum after 10 days of treatment and the general condition was consequently much improved.

One-stage lobectomy—According to M. D. Tyson one-stage lobectomy is the most satisfactory procedure in the treatment of bronchiectasis, and, with present-day methods, is reasonably safe. But for patients in poor general condition, or for those in whom technical difficulties are expected in the presence of unusually extensive adhesions, multiple-stage operations should be employed. Five cases of unilobar bronchiectasis in which one-stage lobectomy was successful are reported. In one case there were very few adhesions between the normal lobe and the chest, and in 2 cases there were no adhesions. None of these 3 patients developed empyema, and in all re-expansion of the lung was prompt. The average period of post-operative hospitalization was 27 days.

Cordey, M. F. (1939) *Bull. Soc. méd. Hop. Paris*, **55**, 1123.

Reisner, D., and Tchertkoff, I. G. (1940) *Amer. J. Roentgenol.*, **43**, 327.

Tyson, M. D. (1940) *New Engl. J. Med.*, **222**, 579.

BRONCHITIS AND BRONCHO-PNEUMONIA

See also B I M P, Vol. II, p. 696, Cumulative Supplement, Key Nos. 202-207 and Surveys and Abstracts 1939, p. 266.

Bronchitis

Treatment

Sulphanilamide and amidopyrine—C. L. Thenebe *et al.*, because sulphapyridine was not then available, were led to experiment with a combination of sulphanilamide and amidopyrine in acute pneumonias. Their method was to give sulphanilamide in doses of 1½ to 1½ grains per pound body weight in patients up to the age of 2 years, and 1 grain per pound in older children. In some cases 2 grains per pound were given for the first few doses. Amidopyrine was given simultaneously in a dosage equal to one-half that of sulphanilamide. With improvement of the patient the dosage was gradually reduced to one-quarter of the original dose and maintained at this level for 2 to 3 days. The average duration of treatment was 6 days, unless toxic effects necessitated discontinuance of treatment, or if the patient failed to respond. This treatment was employed in 20 cases of clinical broncho-pneumonia and lobar pneumonia, in patients of from 5 months to 13 years of age. There were no deaths.

Thenebe, C. L., Hirschberg, M. S., and Bobrow, A. (1939) *Arch. Pediat.*, **56**, 795.

Broncho-Pneumonia

Aspiration Pneumonitis

C. C. Hall reports 15 cases of aspiration pneumonitis, 14 in women during childbirth, with 5 fatalities. The condition may be due to the inhalation of either a solid or a fluid. Broncho-pneumonia is caused, in some cases, when the bronchus is occluded by a large solid mass; death results from the same form of shock as in pulmonary embolism. From this series it might appear that women in parturition are more liable than others to this complication. There is not, however, any obvious reason why this should be so. Possibly pressure on the pelvic floor during delivery induces the woman to inhale more deeply and to vomit more easily. It has been suggested that adequate preparation for anaesthesia is not made in these cases but in the light of emergency surgery during the Great War and at other times, this suggestion is not valid. Hall suggests that, since the stomach empties slowly in pregnant women, they should be given very little to eat shortly before delivery, and that a suction apparatus ready for immediate use should be kept in every anaesthetic room dealing with obstetrical cases. If vomiting occurs the head should be lowered to facilitate the escape of vomited material.

Hall, C. C. (1940) *J. Amer. med. Ass.* **114**, 728.

BRONZING OF THE SKIN

See also B. I. M. P., Vol. II, p. 711 (Cumulative Supplement Key No. 208) and Surveys and Abstracts 1939, p. 267.

Pigmentation due to Physical and Chemical Causes

Following Application of Iron Salts

C. E. Regner reviews the occurrence of pigmentation of the skin after the application of iron salts during the treatment of ivy poisoning. Although there have been many reports of successful treatment without ill-effects, 8 cases of cutaneous pigmentation have followed this therapy. The pigmentation has always been considered permanent and this justifies the report of a case in which the pigmentation, due to iron deposit, disappeared under treatment after persisting for 8 months. A girl, aged 10 years, had been treated for ivy poisoning by the home application of a solution of ferrous sulphate followed by application of buttermilk. This treatment was said to have made the ivy eruption worse, but eventually the dermatitis subsided, leaving numerous brown spots on the chin where the liquids were applied; these remained unchanged for 8 months. On examination there was nothing unusual except about 12 pinhead sized and numerous smaller dark brown spots on the skin over an area of about 1 square inch. The lesions were smooth without any evidence of inflammation or infiltration. Ultra-violet irradiation with a water-cooled lamp was given weekly for 3 months, and during that time the spots appeared to be fading; there were no severe reactions, such as have accompanied attempts to remove tattoo marks. When seen after an interval of 3 months the pigmentation had entirely disappeared and the skin was as smooth as before the episode occurred.

Argyria

Following nasal medication. B. I. Bryant lays stress on the risk of producing generalized argyria from the use of silver as a nasal application, for this accident is not rare and is due to the action of light on silver absorbed through the nasal mucosa; it may become obvious after 4 weeks of regular application. Silver forms a colloidal mass over the mucosa, and so interferes with ciliary action and the discharge of exudates. The author concludes that, after a few weeks, the method is dangerous, results are not better than with other forms of medication.

Bryant, B. I. (1940) *Arch. Otolaryng., Chicago*, **31**, 127.

Regner, C. E. (1939) *Arch. Derm. Syph.*, **40**, 380.

Schamberg's Disease

W. J. O'Donovan reports the after-history of a case of Schamberg's disease, 23 years after it was first diagnosed. In 1916 this man showed a large, deep purple,

port-wine naevus on the right thigh and leg. On his left leg there had then existed for 4 years numerous, pin-head sized, reddish-brown points scattered and in groups, with several brownish macules the size of sixpenny and shilling pieces. The puncta did not fade on pressure, and scaled slightly on stroking. The macules presented the appearance of slight atrophy of the skin, and did not fade on pressure. In 1939, when the patient was 56, the naevus on the right leg was unchanged. The left leg showed in the front, in the middle, 3 vertical ill-defined oval brown splashes, the largest 3 inches and the smallest 1 inch long. Their surface was smooth, and on the dull, faintly-brown background was a stippling of dark brown, pinhead macules. The front of the skin below these lesions was faintly stippled with discrete brown pinhead macules. The smallest lesion was pinkish-brown with a little wrinkling of its surface, this alone itched. The outer side of the calf presented a faint brown dappling, and a roughening of the surface due to recent rubbing. The whole of the skin on the front of the leg was shot through with fine blue and reddish varicosities. The man enjoyed excellent health. It is concluded that, though Schamberg's disease may progress, it can do so favourably, with the passing years.

O'Donovan, W. J. (1940) *Brit. J. Derm.*, **52**, 60

BURNS AND SCALDS

See also B F M P., Vol. II, p. 719, Surveys and Abstracts 1939, p. 267, and p. 10 of this volume

Clinical Picture

Shock

H. M. Trusler *et al.* investigated the shock which results from extensive burns. Fatal shock occurs more commonly in children and usually follows burns involving more than half the surface of the body no matter how superficial the burn may be. The shock may appear soon after the burn or be delayed for a few days. The authors consider that the shock is not due to absorption of toxins from the burnt tissues, and therefore the supposed action of tannic acid in 'fixing' the toxins is fallacious. Shock immediately after the burn is ascribed to loss of fluid from damaged capillaries. Later shock was due to inflammatory processes in the burnt area leading to greater permeability of the capillaries and subsequent loss of fluid. Toxic manifestations accompanying this type of shock are due to the general reaction of the inflammation. Administration of large quantities of fluid during shock may be very dangerous as it upsets the blood-chemistry and may lead to water intoxication. Repeated blood-transfusions and larger quantities of dextrose are a better and more successful method of treatment. A reported case showed that the local application of tannic acid does not reduce the danger of shock from a large burn: a patient was tanned within 2 hours of the burn under ideal conditions, but died in convulsions on the third day. A large amount of fluid was given to the patient resulting in a very low blood chloride and contributing to the cause of death. In another case of extensive burns the general condition of the patient was treated with repeated blood-transfusions and oxygen, care being taken to keep the blood-chemistry as near normal as possible during the critical period of shock and toxæmia. This patient recovered. The authors consider that local treatment should be confined to keeping the wound clean and promoting its rapid healing.

Trusler, H. M., Fegbert, H. I., and Williams, H. S. (1939) *J. Amer. med. Ass.*, **113**, 2207

Treatment

Three-Dye Method

J. B. Devine employed in 27 cases of burns a mixture consisting of a 1 per cent aqueous solution of gentian violet and of brilliant green, and an 0.1 per cent solution of neutral acriflavine. The advantages claimed for this method are that the mixture is inexpensive and keeps indefinitely, it forms a coagulum rapidly, and with only one or two applications, the coagulum being more pliable than that formed by tannic acid, it quickly relieves pain, and, being a powerful combination

of antiseptics, it is more efficient than tannic acid in preventing infection. The technique of use is as follows. No attempt is made to clean up the burnt area. Blisters are snipped off and dead skin is removed, no anaesthetic being necessary. The burnt area is dabbed, painted, or sprayed with the three-dye mixture. A second application after about half an hour is generally given, but is not always necessary. Tanning begins immediately after the first application, the tan formed being less thick, but more flexible, than that produced by tannic acid. Delayed blisters appearing within a few days of the burning should be snipped off, and the dye applied. No dressings are necessary.

Aloes Ointment

J. F. Crewe reported very satisfactory results from the application of an ointment containing aloes to burns and scalds. This ointment consisted of 2 drachms of powdered aloes and 2 drachms of mineral oil mixed in 1 ounce of white vaseline. Preliminary treatment of the burnt area consisted of thorough cleansing, and, if blisters were present, the serum was drawn off with a hypodermic syringe and a small amount of mercurochrome injected into each. The burnt area was then covered with a layer of sterile gauze on which a layer of ointment at least 1/4-inch thick was spread. The dressing was left in position for 2 days, after which it could be readily removed. On removal the surface of the wound had a clean glazed appearance and did not bleed. Further dressings were applied, each being allowed to remain on 2 days, as a rule 4 to 6 dressings were required to secure healing. The author concluded that aloes has some enzymatic action, as pus was digested from purulent surfaces. Infection of the burnt area was negligible, and no unpleasant by-effects were noted.

Warm Moist Air

According to S. Smith *et al.* the treatment of burns by a chemically produced coagulum is not so satisfactory as that of allowing a natural fibrin eschar to form, under which the burn heals. To obtain more nearly natural conditions for healing they treated third degree burns in cats with warm moist air in special chambers and compared the results with other common forms of surgical treatment. The injured area was measured twice a week to ascertain if there was any reduction in size, and was compared with the control series. The burns treated with warm moist air healed sooner than those treated with either picric or tannic acids. The combination of warm moist air with tannic acid and surgical excision did not differ appreciably in the rate of healing. Surgical excision alone gave better results than no treatment at all, but was not so successful as treatment with picric or tannic acids.

'In Children

W. M. Dennison described the treatment of burns and scalds carried out at the Royal Hospital for Sick Children, Glasgow. The essential point in modern treatment is not tannic acid but coagulation. This lessens toxæmia, secondary infection and trauma, is analgesic, conserves the body fluids, and forms a scaffold for the growth of new epithelium. Many coagulants were tried. Picric acid often produces a toxic erythematous rash and is therefore not advised. Cold tea is the best first-aid remedy. The best coagulant, which gives a very rapid, not over-thick coagulum, has been found to be a combination of tannic acid and silver nitrate. For areas where flexibility is required, dettol burn cream No. 4 (tannic acid, fragacanth, and dettol) has been used with satisfaction.

Burns and scalds are treated in a special side ward kept at a constant temperature of 75° F. Since this has been done, sepsis has ceased to be a serious problem. No bed-clothes touch the child and heat is applied with a cage. No dressings are placed over the coagulum. An extensive burn or scald is treated as the most acute surgical emergency. Treatment is done under full anaesthesia, preferably nitrous oxide and oxygen with a little ether. The use of sedatives only increases the incidence of secondary shock. The theatre is kept at 80° F. and only limited areas are uncovered at a time. Cleansing is done with warm saline, unless an oily preparation has been used or there is gross contamination, when soap and ether are employed. Next a 1 per cent watery solution of gentian violet is painted over the raw surface. This is both antiseptic and mildly coagulating, and demarcates the raw area. The surface is

then dried with hot air from an electric hair-drier. Gauze soaked in 5 per cent tannic acid solution is next applied, then 10 per cent silver nitrate solution in the same manner. The surface is then dried with hot air and 1 per cent gentian violet solution again applied. If necessary fluid is given on the table, usually per rectum, but sometimes intravenously. To combat toxæmia (shown by pyrexia, tachycardia, tachypnoea, restlessness, vomiting, and ultimately delirium and coma) attention is paid first to the coagulum, then to support of the liver, and finally to adrenal insufficiency. The coagulum is frequently inspected and moist areas are dehydrated with ether and painted with 1 per cent gentian violet in alcohol, if necessary retanning is carried out. To support the liver, 10 per cent dextrose saline is given intravenously. Biochemical studies in toxæmia are suggestive of adrenal insufficiency, so desoxycorticosterone acetate has been given in 5 mg. doses intramuscularly every 2 hours with encouraging results. Severe sepsis is treated by retanning after cleansing with hypertonic saline, and the use of sulphonamides.

As the result of this treatment, the case-mortality in the last 5 years has been reduced from 19 per cent to about 7 per cent, the incidence of toxæmia from 33 to 15 per cent, and of sepsis from 33 to 6 per cent.

Industrial Burns

Cod-liver oil Wichmann reports favourably on Lochr's method of treating industrial burns by application of cod-liver oil. The thick layer of cod-liver oil ointment is covered with a layer of gauze and with a plaster-of-Paris bandage, even in burns of the face and head. The dressing is changed after 8 days. After 2 or 3 changes the burn has healed. The author has treated more than a hundred cases of severe industrial burns, due to fire and caustics, with entirely satisfactory results.

Systemic Disturbances in Severe Burns

J. R. Elkinton discusses the aetiology and treatment of severe superficial burns. There have been more experimental investigations than clinical researches, but Wilson *et al.* (1938) analysed 65 cases. The two views as to the aetiology are (a) a burn toxin and (b) physical changes, such as rapid concentration of the blood with loss of plasma protein, the capillary permeability being in one direction only into the tissues so that toxin would not be absorbed. From investigation of 4 clinical cases (1 fatal) Elkinton found that all 4 cases showed concentration of the blood or diminution of the plasma volume, as measured by serial haemocrit determinations, and markedly lowered plasma protein. Three of the patients presented symptoms of a definite period of acute toxæmia between the third and sixth days: fever, albuminuria, mental apathy, disorientation, vomiting, tachycardia, cyanosis. Plasma transfusion to make up for the loss of plasma and its protein is the rational procedure, and gave satisfactory results. Physiological saline or 5 per cent dextrose in distilled water, which is often needed to maintain the patient's fluid balance should be given in moderation. Adrenal cortical extract has been employed, in one moribund patient it had a most astonishing effect, but it was also given to the fatal case.

Crews, J. E. (1939) *Ann. Med.*, **22**, 538

Dennison, W. M. (1939) *Lancet*, **2**, 1107

Devine, J. B. (1939) *Med. J. Aust.*, **1**, 924

Elkinton, J. R. (1939) *Bull. Amer. Lab. Phila.*, **3**, 279

Smith, S., Risk, R., and Beck, C. (1939) *Arch. Surg., Chicago*, **39**, 686

Wichmann (1939) *Zbl. Chir.*, **66**, 655. Abstracted in *Journal de Chirurgie* (1939) **54**, 218

Wilson, W. C., MacGregor, A. R., and Stewart, C. P. (1938) *Brit. J. Surg.*, **25**, 826

Special Types of Burns

Cordite Explosion Burns

Tannic acid and dye therapy B. C. Murless employed a combination of tannic acid and aniline dyes in 18 cases of severe septic burns from cordite explosions.

In nearly all the cases the hands and face were burnt. In order of severity the sites involved were the dorsal surfaces of the hands and forearm, the feet and legs, the face, and the back of the neck. These cases were received in hospital 20 hours after a preliminary treatment of tannic acid and flavine dressings without previous cleansing under anaesthesia. When the dressings were removed the burnt areas almost without exception were found to be septic. The burnt limbs were laid on sterile towels and swabbed over with a solution of 5 per cent methylene blue and 1 per cent brilliant green. They were then sprayed with a 20 per cent solution of tannic acid in 1 in 1,000 acriflavine, and the area was dried with an electric hair-drier. No dressings were used. The tannic acid spraying and the drying process were repeated three-hourly by day for the next 48 hours, and the area was occasionally dabbed with the dye mixture. The crust which formed was at first sticky, but soon became hard with the constant use of the drier. From periods of 5 days onwards the crust began to peel or break off at the edges. The edge of the crust as it receded was treated with the dye mixture till only a small central area was left. One patient died of broncho-pneumonia. With the exception of one case in which a skin-graft was necessary, all the cases were ready for discharge within 21 days.

Murless, B. C. (1940) *Brit. med. J.*, **1**, 51.

CAISSON DISEASE

See also B. I. M. P., Vol. II, p. 730, and Surveys and Abstracts 1939, pp. 28 and 270.

Clinical Picture

Bone and Joint Lesions

B. I. Coley and M. Moore drew attention to caisson disease as a possible cause of vague bone and joint pains which may be discovered later as 'silent' areas of aseptic necrosis. The authors described two cases which, on radiological examination, showed lesions which were clinically silent, in addition to evident arthritis. These lesions occurred in the femoral shaft and diaphyses, in the humerus, tibia, and ischium.

H. Gerbis observed numerous cases of caisson disease during a large building undertaking in which heavy work had to be done as deep as 30 m. below water level. Among 216 workmen, 145 cases of caisson disease were noted, symptoms being mainly myalgia and pain in the joints, often combined with temporary paralysis of the limbs. The pain in muscles and joints was often so severe that the patients lay in distress on the floor. In some cases bleeding from the ear and nose, local oedema, oedema of the lungs, and psychoses were observed.

Coley, B. I., and Moore, M. (1940) *Ann. Surg.*, **111**, 1065.

Gerbis H. (1939) *Dtsch. med. Wschr.*, **65**, 1152.

CANCER

See also B. I. M. P., Vol. II, p. 737, Cumulative Supplement, Key No. 212; and Surveys and Abstracts 1939, p. 270.

Pathology and Aetiology

The Carcinogenic Action of Methylcholanthrene

G. B. Mider and J. J. Morton investigated the effect of methylcholanthrene on the production of tumours in a strain of genetically uniform mice susceptible to spontaneous lymphomatosis. Methylcholanthrene 0.5 per cent in commercial benzene was painted twice a week on the skin of 60 dilute brown mice, and 48 developed leucoses which were of 4 types—general lymphomatosis, localized mediastinal lymphoma, extra-medullary myeloporesis, and reticulo-endotheliosis, and the period before spontaneous lymphomatosis occurs was more than halved. Painting 50 control mice with benzene alone gave quite negative results. A. M. Seligman and M. J. Shear report the results of their researches on the experimental production in mice of cerebral tumours by methylcholanthrene. Subarachnoid

injection of methylcholanthrene in mice and rats failed to produce cerebral tumours. But the intracerebral implantation of pellets of 20-methylcholanthrene gave positive results in 13 out of 20 mice, namely 11 gliomas and 2 fibrosarcomas probably of meningeal origin. Pellets introduced subcutaneously in other mice produced sarcomas more rapidly than in the brain. The gliomas bore an interesting resemblance to the forms occurring in man, both cytologically and histologically. 1. Alexander attaches a note on the differential diagnosis of experimentally produced brain tumours and their relation to cerebral tumours in man. He points out that 6 of the 11 gliomas are of the spongio-astrocytic series. Three of the gliomatous growths were of forms comparatively rare in man, namely 1 ependymoma, 1 oligodendroglioma, and 1 pinealoma. Among the experimental series there was a complete absence of a medulloblastoma, possibly because all the implantations were made into the cerebrum, from which medulloblasts have been thought to be absent.

Anoxia and Primary Lung Tumours

J. A. Campbell, by experiments on mice kept in a low oxygen-pressure chamber, showed that anoxia appears to increase the incidence of primary tumours of the lung, but not of other parts of the body, in mice older than 10 months, and may therefore be a factor in the origin of tumour cells. Of the primary tumours of the lung in the mice in the low oxygen-pressure, just more than half were malignant. The numbers are admittedly not large. Most of the previous evidence, but not all, is to the effect that tumour growth is more rapid in a host in favourable conditions as regards general nutrition. The animals in the low oxygen-pressure chamber were allowed to breed, and the growth of their offspring did not differ from that of the controls. The experiments, which were begun on December 9th, 1936, and terminated on September 2nd, 1939, on account of the war, were elaborately controlled; they show that it is possible to acclimatize mice to 13 per cent of oxygen—equivalent to an altitude of 15,000 feet—so that they bred and reared young which grow at a normal rate under this low oxygen-pressure.

Gastric Tumour in Monkeys associated with Parasitic Nematode

C. Bonne and J. H. Sandground, of the Institute of Pathology, School of Medicine, Batavia, Java, give an account of an epithelial tumour, bordering on malignancy, in the stomach of the common Javanese monkey (*Macacus mordax*) due to the presence of a small nematode worm *Nochitia nochti*. Among 68 monkeys examined 6 were found to show the presence of a hyperaemic cauliflower-like mass usually at about the junction of the fundus and the pre-pyloric area of the stomach. Superficially a benign papilloma, it was shown histologically to invade the muscularis mucosae. In each tumour 11 to 23 worms were found. In 2 monkeys thought to be free from this infestation the stomach was opened and found to be normal; a number of living *Nochitia nochti* worms were then introduced, in both these animals the tumours were found within 2 months. As the original description of the nematode by I. Travassos and F. Vogelsang appeared in a Brazilian journal which is not widely available, a full account is given in this article. The authors do not make any suggestion that this nematode has a bearing on gastric cancer in man.

Diet

Fritz Biscoff and M. Louisa Long present a preliminary report on the influence of various dietary constituents on somatic and tumour growth in mice of the Marsh-Buffalo strain inoculated with sarcoma 180. It had previously been shown that calorie restriction, without any deficiency in essential nutrient factors or certain amino-acids, influenced the rate of tumour growth. In the present experiments a vitamin-free basal diet was chosen on which the mice rapidly lost weight and appetite, and tumour growth was markedly retarded, in some cases inhibited.

The effect on somatic and tumour growth was observed when the following substances were added to the basal diet: vitamins B₁ and B₂ (administered parenterally), nicotinic acid, Galen B (a preparation of the whole vitamin B complex containing B₁, B₂, B₆, nicotinic acid, and the filtrate factor), cystine, and the unsaturated fatty acids; in one experiment gelatin was substituted for the casein of the synthetic diet, calorie restriction was also superimposed in others. The authors conclude that growth of sarcoma 180 is not significantly influenced

by the exogenous supply of tyrosine, tryptophane, vitamins B₁, B₂, or nicotinic acid. Vitamins B₁ and B₂ have a profound effect upon the nutritional state as indicated by calorie consumption and somatic growth, but the deficiency they remedy is not a factor in tumour growth. The experiments indicated that some specific factor in the vitamin B complex (Galen B) appears to accelerate tumour growth, suspicion resting on B₆ or the filtrate factor.

Intranuclear Inclusion Bodies in Carcinoma of the Thyroid Gland

C. F. Stewart described inclusion bodies, multiple in some and large in other nuclei of the carcinomatous cells of a thyroid tumour. These inclusion bodies gave the staining reactions of known virus inclusion bodies. Assuming that these characteristic inclusions indicate the presence of a virus, the question arises whether the hypothetical virus has any causal relation to the tumour or whether the virus was secondarily implanted in the carcinoma. In favour of the aetiological relation is the known association of viruses with some animal tumours, such as the Shope rabbit fibroma, infective myxomatosis of rabbits, and the renal adenocarcinoma of frogs. Further, in 38 other cases of thyroid carcinoma Stewart found these inclusion bodies in 10. On the other hand, it has been shown that a spontaneous transplantable rabbit tumour may become secondarily infected with virus III (Pearce and Rivers).

Abortifacient Action of the Serum and Urine from Patients with Cancer

T. H. Elsasser and G. B. Wallace described the abortifacient action of the blood serum and urine of patients with cancer when injected intravenously into pregnant rabbits. The uterine changes thus produced were progressive placental necrosis with an infiltration of inflammatory cells, and early in pregnancy there was a rapid loss in the structure of the retained foetus. In non-pregnant female rabbits the urine or serum of cancerous patients produced degeneration and destruction of the granulosa-celled portion of the Graafian follicles, leading to sclerosis of the ovaries, injection into normal male rabbits was followed by degeneration of the testes resulting in complete absence of the spermatogenic process. K. W. Thompson *et al.*, of the Surgical Department of the Yale University School of Medicine, repeated these experiments, they obtained blood serum and urine from 6 undoubted cases of malignant disease and also from 6 patients free from any evidence of cancer. The urine or serum of the majority of the tested cancer patients contained a principle which caused the termination of early pregnancy in rabbits. But the principle was not specific for cancer because 3 of 6 apparently non-cancerous patients had this agent in the blood or urine, and one of the cancer subjects did not show it in either serum or urine. The changes induced in the rabbits were generally confined

Alexander, L. (1939) *Amer. J. Cancer*, **37**, 395.

Biscoff, F., and Long, M. L. (1939) *Amer. J. Cancer*, **37**, 54.

Bonne, C., and Sandground, J. H. (1939) *Amer. J. Cancer*, **37**, 173.

Campbell, J. A. (1940) *Brit. med. J.*, **1**, 336.

Elsasser, T. H., and Wallace, G. B. (1939) *Science*, **89**, 250.

Mider, G. B., and Morton, J. J. (1939) *Amer. J. Cancer*, **37**, 355.

Pearce, L. L., and Rivers, T. M. (1927) *J. exp. Med.*, **46**, 81.

Seligman, A. M., and Shear, M. J. (1939) *Amer. J. Cancer*, **37**, 364.

Stewart, C. I. (1939) *Amer. J. Cancer*, **37**, 196.

Thompson, K. W., Hale, T., Jr., and Whitcomb, B. B. (1939) *Amer. J. Cancer*, **37**, 233.

Travassos, L., and Vogelsang, F. (1929) *Sci. Med.*, **7**, 509.

Prognosis

Skin and Lip Cancer

S. Peller, writing on the expectancy of life and the mortality from skin and lip cancer, analysed 715 cases from the histories of patients with squamous-celled carcinoma of the lip and cheek between 1921 and 1931, and also of those with that growth on the eyelids between 1921 and 1929, irrespective of whether or not they received treatment. At the onset of the disease, patients with epithelioma of skin or lip were about the average age of all other cancer patients, but at the time

of death they were older. The influence upon the expectation of life and mortality depended on the age at onset. Patients under 60 years of age with cancer of the skin and lip had an increased mortality and a shortened expectation of life, as compared with the average population at the same age. Cases with onset at ages above 70 showed a lower mortality, and a higher expectation of life.

Peller, S. (1940) *Amer. J. med. Sci.*, **199**, 499.

Treatment

Radiotherapy

R. Paterson assessed the value of radiotherapy, including both radium and deep X-rays, in the treatment of cancer. He also divided malignant disease into groups according to its relative curability. The first group included carcinoma of the skin, breast, mouth, uterus, and vagina. This group was called the 'curable' group because, especially in the early stages, many patients are cured. In the second 'treatable' group was placed malignant disease of the stomach, intestine, prostate, rectum, bladder, ovary, and larynx; these may be treated surgically, and a cure may follow in early stages, or by radiotherapy with which the same result may be obtained, but lastly, most of the cases call for radiotherapy as a palliative. In the 'incurable' group were included carcinoma of the liver, pancreas, lung, and oesophagus; no form of treatment gives any hope of cure in these cases. Radiotherapy was contra-indicated in carcinoma of the alimentary tract, connective-tissue sarcomas, and most cases of advanced malignant diseases. Sarcomas, however, may be temporarily alleviated by radiotherapy, but their treatment is primarily surgical. Carcinomas of the bladder, larynx, and brain rarely respond to radiotherapy, but it is most useful in this series as a palliative measure. In the treatment of embryonal primitive cell tumours of unknown origin, and reticulo-endothelial tumours, radiotherapy is valuable as they are extremely radio-sensitive. Even so the standard of cure is not high, but it is desirable to use this treatment as they do not respond to surgery. Radiotherapy is the treatment of choice in malignant tumours of moderate sensitivity in accessible sites, such as the lips and anus. It may also be combined with surgical measures with advantage in carcinomas of the breast, uterus, and mixed parotid tumours. Paterson laid stress on the importance of early diagnosis and, above all, early energetic treatment of malignant disease in order that more cases may be cured. This calls for co-operation between the public and the doctor.

Paterson, R. (1939) *Brit. med. J.*, **2**, 904.

CANCERUM ORIS

See also B. L. M. P., Vol. II, p. 749; and Cumulative Supplement, Key No. 213.

Antigangrene Serum

A. Fekstein, reviewing 40 cases of noma, pointed out that most of these occurred during the hot months of the year. Of 9 patients treated with local applications of neoarsphenamine powder, accompanied by the intravenous injection of 0.15 g. neoarsphenamine daily, 8 showed rapid progression of the necrotic process, and a fatal termination. One patient in an early stage with very limited necrosis, showed amelioration after the second injection, and recovered. Surgical extirpation was unsuccessful in one case. The author then tried gangrene antitoxin, injecting 10 to 20 c.cm. into the healthy tissue adjacent to the necrotic area. At the same time 10 to 20 c.cm. of the antitoxin was injected intramuscularly, and an equal amount intravenously. This treatment was repeated daily, and was continued until sloughing of the necrosed tissues occurred. By this time, on an average, 500 c.cm. of antitoxin had been given to 21 patients, in more or less advanced stages. Treated thus, 11 progressed to complete recovery, and in these patients signs of demarcation were noticeable after the first local injection. In some of the remaining 10 cases temporary improvement occurred, but later the patients relapsed and died. The other patients were in the terminal stages of the disease, and died soon after admission to hospital.

Eckstein, A. (1940) *Amer. J. Dis. Child.*, **59**, 219.

CATARACT

See also B.E.M.P., Vol. III, p. 1, and Surveys and Abstracts 1939, p. 272

Aetiology*High-Tension Electric Current*

O Knusel described 2 cases of injury by high-tension current leading to lens opacities lying immediately beneath the lens capsule and appearing shortly after the accident; in a third case, in which the patient was struck by lightning, the immediate result was paralysis of the limbs which gradually disappeared. 18 years later, when the patient was 38 years of age, lenticular opacities appeared.

Inhalation of Para-dichlorobenzene Vapour

M. I. Berliner reported 2 cases of para-dichlorobenzene poisoning associated with loss of weight, jaundice, and the formation of cataracts. One was a woman aged 27 years and another aged 25. Both had been exposed to the fumes of the chemical. The drug is used commercially in the cleaning of clothes and furs and in the preparation of 'moth-bags'. The general symptoms of both patients disappeared when they were removed from the effects of the drug. In the first case the cataracts were sufficiently developed to warrant extraction, after which the vision improved. In the second case the lens opacities remained stationary after ingestion of the fumes stopped. Berliner investigated the effect of the drug on rabbits and guinea-pigs. When the vapour was inhaled, vacuolation and necrosis of the liver cells occurred. When it was given by mouth to 1 rabbit, lenticular opacities occurred in the eyes. That proper liver function is essential to the metabolism of the lens has been shown by many workers. For example, glutathione, necessary for proper oxidation in the lens, is not formed if the liver is not functioning properly. Acidosis accompanying severe liver damage changes the pH of the aqueous and therefore affects the permeability of the lens capsule. Berliner concluded that this drug is toxic to human beings and therefore a warning of its toxic properties should be given when it is sold.

Berliner, M. I. (1939) *Arch. Ophthalmol.*, N.Y., **22**, 1023.

Knusel, O. (1939) *Schweizer med. Wschr.*, **69**, 1084.

Treatment*Pre-operative Injection of Typhoid-H Antigen*

C. A. Noe investigated the effects of foreign-protein therapy on post-operative ocular inflammations in a group of 150 patients after operation for senile cataract. Brown had advocated the intravenous use of typhoid-H antigen in cataract extraction as a prophylactic. According to this author an appreciable (1:100) blood titre of antibodies should be built up before the anterior chamber of the eye is opened. By injecting intravenously the flagellar-H antigen of 15 million typhoid organisms Brown obtained blood typhoid titres of 1:100 and within 48 to 50 hours after injection. In the present study the foreign-protein substances used were omnadin and typhoid-H antigen. Omnadin is described as 'a sterile solution composed of protein substances obtained from nonpathogenic bacteria (*Sarcina* and *B. mycoides*), various animal fats and lipoids derived from bile'. Fifty patients received no foreign-protein therapy, 50 received 4 consecutive daily intramuscular injections of 2 c.c.m. of omnadin, the remaining 50 received 4 intravenous injections of typhoid-H antigen each made from 15 million organisms. Patients in each of the 3 groups were observed simultaneously so that seasonal influences were eliminated. Operative trauma was similar in the 3 groups: 74 per cent, 70 per cent, and 66 per cent respectively of the 3 groups were operated on by the intracapsular method. The eyes were inspected daily for 12 days after operation and the amount of ciliary injection was noted. The omnadin group showed the greatest reaction; the control group but slightly less; the typhoid group fell definitely below the other two. The omnadin and control groups showed no rise in temperature; in the typhoid-H antigen group a definite temperature response was observed with the peak from 4 to 8 hours after injection. The specific antibody response in the blood was studied

in 14 cases, no appreciable titre was obtained until about the fifth day maximum usually not before the ninth day; the O agglutinins usually rose more rapidly than the H.

The author concludes that apparently intravenous administration of ty antigen lessens the inflammatory reaction after cataract extraction. There is no definite relation between blood-antibody titre and post-operative. The author states that typhoid antigen must be used with care in old pathological vascular systems.

Brown, A. I. (1938) *Arch. Ophthalm.*, **N** 3, 19, 181.

Noe, C. A. (1939) *Amer. J. Ophthalm.*, **22**, 1014.

CEREBROSPINAL FEVER

See also B. I. M. P., Vol. III, p. 39, Cumulative Supplement, Key No. 2. Surveys and Abstracts 1939, pp. 125 and 274.

Clinical Picture

Chronic Forms

A. W. Stott and W. S. C. Copeman report 17 cases of chronic meningitis without meningitis in the British Expeditionary Force in during the prevalence of cerebrospinal fever for 9 weeks. Support is given the view that, though sporadic cases of chronic meningococcal septicaemia are rare, it becomes commoner whenever cerebrospinal fever is prevalent. The picture of chronic meningococcal septicaemia is probably often overlooked, and as in these 17 cases, as subacute rheumatism, influenza, or trench fever cases are tabulated, and mention is made of 10 more cases, of which the picture is so characteristic that it justifies the diagnosis. The onset is usually acute with fever, severe headache, migratory pains in joints and muscles a few days later one or more of several forms of skin eruption appear, the most being pink or red macules, papules and nodules which may be tender and petechial. There is fever, from 100 to 105 F., intermittent or continuous, which, if untreated, may persist for weeks, months, or longer. The patient shows a remarkable freedom from debility. The complications include endocarditis, nephritis, and epididymitis. Sulphapyridine in moderate doses at the mouth terminates the disease in a dramatic manner; 15 cases were thus cured and all manifestations of active disease disappeared in 24 hours.

Stott, A. W., and Copeman, W. S. C. (1940) *Lancet*, **1**, 1116.

Treatment

Sulphonamide Compounds

O. Sprockhoff reports on the treatment by prontosil of 15 cases of meningitis. 2 died, 1 developed hydrocephalus, and 12 were cured. All received prontosil album (sulphanilamide), 3 also received injection of meningococcus serum and 1 had a blood transfusion. No damage was produced by prontosil. Half a tablet (1 tablet = 0.3 g. prontosil album) was given 3 times a day to infants below the age of 1 year for 3 days. Infants between 1 year and 3 years received a whole tablet 3 times a day for 3 days, children 3 to 6 years 1½ to 2 tablets 3 times a day for 3 days, children from 6 to 14 years 2 to 3 tablets 3 times a day. This course was repeated if necessary after an interval of 3 to 5 days. Double these doses were given as a suppository if the tablet could not be taken orally. In 2 cases examination of the cerebrospinal fluid showed improvement on the third day of treatment, the number of cells being decreased. Cerebrospinal fluid was withdrawn as a therapeutic method at intervals of 3 days or more, according to the general condition of the patient. Results were much better than those of other authors who did not use prontosil.

F. Hoppe treated 58 cases of meningococcal meningitis with prontosil; 39

received prontosil only by mouth; 19 received, in addition to prontosil orally, injections of sheep serum and of prontosil

The author gave 2 tablets each of 0.3 g. of prontosil 3 times daily to infants, and 3 tablets 3 times daily to older children. This was given for 10 days, after an interval of 4 days 1 tablet was given 3 times daily for another 10 days

Lumbar puncture was performed daily or every second day and, after improvement of the general condition, once a week. In 10 cases a blood transfusion was necessary. Of the 39 treated exclusively with prontosil orally 31 were cured after an average dose of 115 tablets of 0.3 g. A mortality of only 20 per cent is considered a great improvement. Only a few cases showed side effects from the prontosil, namely cyanosis, exanthema, and jaundice

Serum and Sulphapyridine Compounds

J. H. Jordan *et al.* reported 160 cases of cerebrospinal fever which were divided into 4 treatment groups. Of the patients, 50 received serum, and 50 sulphapyridine, while 30 of them received both these treatments and 30 others had sulphapyridine and antitoxin. A total dose of 20 g. of sulphapyridine was given in this series. If there was no clinical improvement the dose was increased. Serum was given every time a lumbar puncture was performed, i.e. every 24 hours after the first 12 hours. Twenty c.cm. of antitoxin was given intravenously and intramuscularly to the fourth group on admission. The intramuscular dose was repeated in 12 hours and again if necessary. The results in this series were good. The fatality-rate in Group I was 38 per cent, in Group II 32 per cent, in Group III 26.6 per cent, and in Group IV 20 per cent. Sulphapyridine was therefore of more value when combined with serum or antitoxin. Of 126 cases 100 had positive blood-cultures but only 21 of these cases were fatal. The concentration of the drug in the cerebrospinal fluid was found to bear little relation to the dose. There were no toxic reactions in this series.

Hoppe, T. (1939) *Dtsch. med. Wschr.*, **65**, 1194

Jordan, J. H., Blakelock, J. H., and Johnston, W. R. (1940) *Brit. med. J.*, **1**, 1005

Sprockhoff, O. (1939) *Dtsch. med. Wschr.*, **65**, 1079

CERVICAL RIB

See also B.F.M.P., Vol. III, p. 75, and Surveys and Abstracts 1939, p. 277

The Scalenus Muscle Syndrome

R. H. Patterson stated that, during inspiration, the scalene muscles may exert pressure or accentuate rib pressure on the brachial plexus and the subclavian vessels. The chief complaint of the patient is pain of varying intensity in any part of the neck, shoulder, or upper extremity. He advises division of the anterior and medial scalenus muscles, and removal of the rib, if present. He also suggests division of the anterior scalenus through the muscle belly, so as to avoid the pleura.

Patterson, R. H. (1940) *Ann. Surg.*, **111**, 531

CHANCROID

See also B.F.M.P., Vol. III, p. 97, Cumulative Supplement, Key No. 227, Surveys and Abstracts 1939, pp. 155 and 277, and p. 91 of this volume

Treatment

Sulphanilamide

Since sulphanilamide is effective in the destruction of the haemolytic streptococcus, W. F. Schwartz and H. E. Freeman considered that it might be of use in the treatment of conditions due to the haemophilic streptobacillus of Ducrey. They reported 37 cases of chancroid so treated, and compared them with 60 similar cases treated by other methods. The average daily dose of sulphanilamide was 46 grains. Blood-level determinations and the clinical progress showed that a high maintenance dose was the best method of treatment. The average duration of the disease

in the treated group was 32 days and in the control group 35 days. Healing took an average of 32 days in the control group, but required only 15.7 in those who were treated with sulphanilamide. Chancroidal ulcers responded best to the treatment, then unruptured buboes. Ulcers on the glans penis were the most resistant.

A. Baccaredda also reported on treatment of Ducrey's streptobacillosis with sulphanilamide. In all the cases vaccines were used first, but it soon became apparent that treatment with sulphanilamide was simpler and more effective, as it succeeded in 100 per cent of cases. The author found that a high dosage of sulphanilamide was necessary to give initial results and fairly high doses were necessary to effect a complete cure. Side effects were negligible and the author pointed out that patients should be under medical observation all the time as sulphanilamide had to be discontinued if severe toxicosis developed.

Baccaredda, A. (1939) *Dermosiflografo*, **23**, 1231.

Schwartz, W. F., and Freeman, H. E. (1940) *J. Amer. med. Ass.*, **114**, 946.

CHICKEN-POX

See also B F M P, Vol. III, p. 103

Diagnosis and Differential Diagnosis

From Herpes Zoster

I. P. Barker gives reasons for thinking that herpes zoster and chicken-pox are not the same condition. Herpes is non-infectious, whereas chicken-pox is highly so, chicken-pox, unlike herpes, may be accompanied by pyrexia, whereas chicken-pox practically never has any complications affecting the central nervous system, herpes presents definite pathological changes, such as a large increase in lymphocytes in the cerebrospinal fluid or motor symptoms perhaps indicative of pyramidal-tract involvement, as recurrence of either condition is unlikely, it is strongly suspicious that herpes may occur in those who had chicken-pox in their youth, chicken-pox usually attacks those under 10, whereas herpes generally affects people over that age, and herpes is often seen in localities where chicken-pox is unknown.

Barker, I. P. (1939) *Arch. Derm. Syph., N.Y.*, **40**, 974

CHORIONEPITHELIOMA AND HYDATIDIFORM MOLE

See also B F M P, Vol. III, p. 216.

Diagnosis

Quantitative Friedman Test

F. J. Schoeneck described a fractional Friedman test which formed the basis of a quantitative test. He estimated the smallest quantity of urine that would give a positive test for a given stage of pregnancy. Three out of 7 cases of hydatidiform mole gave a positive test for high dilutions of urine, all showing the active vesicular type of mole. The other moles, in which more urine was required to produce a positive test than the average for this stage of pregnancy, were 'fleshy' in type or contained fewer vesicles. Three cases of chorionepithelioma, all of which ended fatally, were investigated. The test was positive, and the quantitative test is most useful in this condition in determining the prognosis. Two of these cases followed hydatidiform mole. Every patient with such a mole should be tested every month for at least a year after its expulsion. If it remains positive for longer than a month or two, or if a higher dilution becomes positive, the patient should be curetted for diagnosis. Multiple pregnancy and hyperemesis gravidarum also give positive reactions in high dilution, so they, as well as the above conditions, must be borne in mind when this result is obtained.

Schoeneck, F. J. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 485.

Hydatidiform Mole

Criteria of Malignancy

B. Tenny and F. Parker made a study of 12 cases of hydatidiform mole in order to determine some criterion of the development of malignant chorionepithelioma. All the patients were admitted to hospital because of bleeding between the second and sixth months of pregnancy; 2 cases developed malignant epithelioma. It is extremely important clinically to determine the onset of malignant invasion. There are no histological criteria based on microscopic sections of a mole to determine whether it is potentially malignant. However, hormonal determinations may give a fairly accurate diagnosis. The amount of urinary prolactin gave no guide in the 12 cases investigated, 7 cases, including one which became malignant, showed an increase while 5 cases, including the other malignant one, showed a normal or low amount of prolactin in the urine. The amount of prolactin found in the urine corresponds roughly to the amount of active trophoblastic cells in the placenta or mole, and this is not necessarily related to its malignant potentialities. In following the cases in this series weekly Aschheim-Zondek tests were done.

Light benign cases had a negative test at the end of two weeks after delivery of the mole, in 2 others the test was negative at the end of 4 weeks, no benign case stayed positive after 4 weeks. The authors conclude that all cases should have a negative Aschheim-Zondek test within 4 weeks of delivery of the mole, and a positive test 6 weeks or longer after passage of a mole indicates the need for surgical intervention.

Tenny, B., and Parker, F. (1939) *New Engl. J. Med.*, **221**, 598.

Chorionepithelioma

In a Virgin aged 71

G. Maizels reported a case of probable chorionepithelioma in a virgin of 71 years of age. The patient was admitted to hospital with a pelvic tumour and a history of vaginal haemorrhage, two or three days a week, with intermittent aching pains in the abdomen. Because the hymen was intact, a vaginal examination was made under a general anaesthetic. The condition of the vulva, cervix, and vagina was consistent with virginity, and on palpation of the posterior fornix a hard fixed mass, connected with the uterus, was discovered. The patient's condition became worse, and she died. At necropsy the uterus was found to be enlarged, with two subserous metastases on the anterior surface. The pouch of Douglas was completely filled by a soft necrotic tumour spreading from the uterus, and the right tube and ovary were buried in the tumour, but were not enlarged. Microscopical examination showed that the preponderant cells of the tumour were syncytial, large multinucleated masses of cytoplasm were scattered throughout the section and exhibited a considerable degree of polymorphism. Extensive areas of haemorrhage were common. A diagnosis of chorionepithelioma was made largely on the histological findings. The most reasonable explanation appeared to be that the tumour originated from a teratoma of the uterus.

Maizels, G. (1940) *Lancet*, **1**, 690.

CLIMACTERIC AND ITS DISORDERS

See also B.E.M.P., Vol. III, p. 228; Cumulative Supplement, Key Nos. 242 and 243, and Surveys and Abstracts 1939, p. 279.

The Climacteric in the Female

Hyperthyroidism as Cause of Symptoms

J. A. Huet and A. D. Herschberg consider that hyperthyroidism is usually responsible for the vasomotor disturbances at the menopause. This can be demonstrated by increase in the basal metabolism or by appreciable enlargement of the thyroid. There is usually hyperfolliculinaemia, a raised cholesterol level, and uraemia; Aron's test, which shows an increased amount of thyrostimulin, is usually

positive. The anterior pituitary plays the controlling part in the chain of events leading up to menopausal disturbances. Iodine treatment, di-iodothyroxine, and vitamin A are given at first, hormone therapy, namely large doses of folliculin, are given for intense vasomotor disturbances; the male hormone is reserved for the treatment of polyadenomatosis. Medical treatment is not often sufficient; the method of choice then is radiotherapy of the pituitary region by the following technique: with 150-180 kv and 8 mm aluminium filtration, 8 fields are irradiated, namely the 2 temporal, frontal, sino-maxillary, and maxillary angle fields, a dose of 225 r is administered to each field 3 times a week, with a maximum of 8 sittings. Over 90 per cent good results are claimed with this method.

Treatment

Stilboestrol.—J. Huberman and M. J. Colmer report the effect of stilboestrol on the menopausal symptoms of 77 women. Of these 57 per cent were physiological menapauses, 33 per cent surgical, and 10 per cent the result of radium treatment. The drug was given hypodermically, orally, and, in those with pruritus vulvae, per vaginam. It was active by all 3 routes, hypodermically, 0.2 mg. 3 times a week for 6 weeks relieved the symptoms, doses as high as 5 mg. being sometimes given. Of the patients 90 per cent were improved by the treatment. An 'oestrus' type of vaginal smear took the place of the menopausal type. Vaginal bleeding occurred in 20 patients. The treatment should be continued until the symptoms disappear, and can be resumed if a relapse occurs.

Oestradiol dipropionate.—I. M. Dorr and R. R. Greene treated 60 menopausal women with oestradiol dipropionate and reported the results obtained in 55 of them. Of the many menopausal symptoms all the patients treated were alike in suffering from hot flushes. A note of the frequency and severity of the hot flushes was kept as an index of the success of the treatment. The average age of the patient was 43 years. In 29 of them the menopause was physiological and in the rest surgically induced. The drug was given in large doses, 2.0 to 5.0 mg. per week at first, by intramuscular injection. The dose was then reduced to find the maintenance dose on which the patient remained free from symptoms. The results of this treatment were compared with those of oestrone by substituting oestrone for the drug in 11 cases. Ten of these patients had a recurrence of menopausal symptoms when receiving oestrone. Oestradiol dipropionate also yielded the oestrus type of vaginal smear which regressed to the menopausal type if oestrone were given instead. The authors concluded that oestradiol dipropionate is of value in the treatment of the menopause and is clinically more effective than oestrone.

Testosterone propionate.—D. Silberman *et al.* treated 15 menopausal women with testosterone propionate. In 2 cases the menopause was surgically induced. The dosage was 5 mg. given subcutaneously 2 or 3 times a week. When the condition improved a maintenance dose of 5 to 10 mg. by mouth, combined with bile salts, was given. The best method of administration was, however, found to be the implantation of 25 mg. pellets of the crystalline substance under the skin. In all cases symptoms such as hot flushing, sweating, and fatigue were relieved. In 2 patients suffering from arthralgia as well as other menopausal symptoms oestradiol dipropionate was alternated with testosterone, with successful results.

Implantation of theelin pellets.—H. G. Bennett *et al.* treated 21 menopausal women by subcutaneous implantation of compressed crystalline theelin pellets. In a single implantation, 3 to 10 pellets with a total weight of 8 to 50 mg. were employed. Several patients, of whom 13 were physiological, 6 operative, and 2 the result of irradiation, had two or more implantations. Oestrogen and follicle-stimulating hormone assays were made on the urine of the patients before and during treatments. In 10 patients vaginal biopsies were similarly studied. In all cases the urinary oestrogen level rose following the implantation. The follicle-stimulating hormone level fell in all but 5 cases. The pellets ended the atrophy of the vaginal mucosa in the 10 cases investigated. It increased its growth with thickening of the squamous layer and mitotic figures in the basal layers. In 18 patients subjective symptoms disappeared after implantation, but the duration of this improvement varied. A second implantation, however, rendered them symptom-free again in most cases. The other 3 patients were only improved by the therapy. There was no constant relation between the hormone level in the urine, the changes in the vaginal mucosa,

and the presence of symptoms. There were no unpleasant effects in this series at the site of implantation. No uterine bleeding or breast changes were produced. This method of treatment is recommended as being easy and because it is a good method of giving oestrogenic hormones in a way that allows them to be absorbed over a long period.

Bennett, H. G., Biskind, G., and Mark, J. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 504

Dorr, L. M., and Greene, R. R. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 458

Huberman, J., and Colmer, M. J. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 783

Huet, J. A., and Herschberg, A. D. (1939) *Monde méd.*, **49**, 691

Silberman, D., Radman, H. M., and Abarbanel, A. R. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 332

The Climacteric in the Male

Treatment

Testosterone propionate H. B. Thomas and R. T. Hill stated that the male climacteric may pass unnoticed or it may be characterized by absence of libido or depressive melancholia of the involutional type. Many androgenic substances have been given to increase libido but little has been done in the treatment of the melancholia. The authors treated 2 cases with testosterone propionate: 10 mg. once, twice, or 3 times a week were given for a few weeks and a remarkable improvement occurred in both cases. Seven and 10 months after treatment the patients were still well.

Thomas, H. B., and Hill, R. T. (1940) *Endocrinology*, **26**, 953

COLITIS

See also B. F. M. P., Vol. III, p. 292, Surveys and Abstracts 1939, p. 286, and p. 26 of this volume

Ulcerative Colitis

Clinical Picture

Associated with infantilism S. Davidson reports 3 cases of infantilism in chronic ulcerative colitis. Though this is common in idiopathic steatorrhoea and coeliac disease, no previous record in ulcerative colitis could be traced by the author. The first patient started the disease at the age of 12 years, and when seen 5 years later still appeared to be 12. The left testis was undescended, the penis infantile, and the secondary hair undeveloped. He died shortly afterwards of broncho-pneumonia. The second patient started bloody diarrhoea at 13 years, having always been small of stature. This continued, with intermissions, until he was 15, when he was found to be infantile. He continued in poor health and died at 17, still infantile with a high-pitched voice, and no primary or secondary pubertal changes. At necropsy, the anterior pituitary showed vacuolation of the nuclei of the cells, increase in basophil cells, many large chromophobe cells, and colloid follicles in the anterior lobe. Case 3 resembled case 2 but was ultimately discharged somewhat improved though still infantile. It was thought likely that these were examples of secondary infantilism, due to faulty absorption of food. The basophilic pituitary hyperplasia was similar to that in animals with hypovitaminosis A and F.

Treatment

Prontosil soluble. -A. E. Brown *et al.* employed neoprontosil (prontosil soluble) orally in 48 cases of chronic ulcerative colitis. Of these, 19 patients received, in addition to the neoprontosil, either vaccine or serum therapy. In the group receiving neoprontosil alone, 44.8 per cent showed excellent clinical results, 44.8 per cent showed fair results, and 10 per cent showed poor, or no, results. In the group receiving neoprontosil and vaccine or serum therapy, 42 per cent showed excellent results, 32 per cent fair results, and 26 per cent poor, or no, results. The dosage of neoprontosil was 4 to 5.5 g. daily, divided into 5 doses. A course lasted for from 10 to 14 days. In some cases a second course of 2.5 g. daily for 10 to 14 days was given, with an interval of 14 days between courses. Results considered as excellent

comprised a symptomatic and proctoscopic inactivation of the disease. The authors considered that the use of neoprontosil was justifiable in the treatment of chronic ulcerative colitis, and was better than that of sulphanilamide because of the toxic effects sometimes occurring with the latter

Brown, A. F., Herrell, W. L., and Bergen, J. A. (1939) *Ann intern Med.*, **13**, 700

Davidson, S. (1939) *Arch intern Med.*, **64**, 1187

COLON, CARCINOMA OF

See also B. F. M. P., Vol. III, p. 317, and Surveys and Abstracts 1939, p. 288.

Morbid Anatomy

Polyposts

Six workers at the Mayo Clinic have made contributions to the subject of polyposis of the colon and rectum, especially in relation to subsequent carcinoma. H. M. Weber refers to A. C. Broders' term polypoidosis (Menetrier's *poli-adénomes-en-nappe*) which though probably similar from a pathological aspect to polyposis differs greatly in its gross appearance, the mucosa being transformed wholly or in part into a plaque-like mass of polypoid structures and contrasting with the appearance of the discrete sessile or pedunculated masses with normal or nearly normal mucosa between the lesions in polyposis (Menetrier's *poli-adénomes polypeux*).

J. A. Bergen classifies polypi into (a) inflammatory, following severe chronic ulcerative colitis and chronic ulcers, and (b) adenomatous, but inflammatory polypi may become adenomatous and eventually carcinomatous. The hereditary, congenital, and familial characters of multiple polypi are emphasized. As Bergen remarks, there is only a short step between the formation of polypi and of carcinoma, carcinoma of the colon, when it recurs, does not necessarily do so at the site of resection, but in another segment of the colon near the portion resected.

During 15 years a diagnosis of single or multiple polypi of the colon and rectum was made at the Mayo Clinic in 42 infants and children, nearly half the patients being 4, 5, or 6 years when first seen. R. L. J. Kennedy found that 27 were boys and 15 girls, and that in 27 a single polypus only was present. Material for histological examination was obtained from 15 patients, there were 6 cases of adenoma, adenocarcinoma grade 1 in 7, adenocarcinoma grade 2 in 1, and 1 of a reticulum-celled lymphosarcoma. In other cases the growth had been destroyed by fulguration.

R. B. Phillips records cases illustrating the following points: the value of periodical examination of the colon in patients who have had a growth there removed, as a fresh adenoma may arise in the colon and become malignant; prophylactic surgery in removal of polypi, the occurrence, fulguration, and recurrence of polypi in the left portion of the colon, necessitating left hemi-colectomy which brought to light grade 1 carcinoma in several polypi and 1 small polypus with grade 2 carcinoma; and carcinomatous change in congenital polyposis. Fulguration has been the most adaptable and satisfactory method of destroying polypi. N. D. Smith has found the monopolar or Oudin current to be the best, especially when it is supplied by an apparatus which will permit separate control of the spark gap and the voltage. A sigmoidoscope provided with an accessory tube for removal of the smoke due to fulguration has been useful. Haemorrhage may follow fulguration. C. F. Dixon regards all polypi of the colon and rectum as precancerous, even though biopsy may show freedom from carcinoma; he considers that a single polypus of the colon or rectum can be excised locally if it has a pedicle, sessile polypi usually require a more radical procedure, such as segmental resection.

Bergen, J. A. (1940) *Proc. Mayo Clin.*, **15**, 105

Dixon, C. F. (1940) *Proc. Mayo Clin.*, **15**, 109.

Kennedy, R. L. J. (1940) *Proc. Mayo Clin.*, **15**, 108.

Menetrier, P. (1888) *Arch. Physiol. norm. et path.*, s. 4, **1**, 32

Phillips, R. B. (1940) *Proc. Mayo Clin.*, **15**, 97

Smith, N. D. (1940) *Proc. Mayo Clin.*, **15**, 101

Weber, H. M. (1940) *Proc. Mayo Clin.*, **15**, 101

Treatment

Caecostomy

F. W. Rankin advocates caecostomy as a valuable adjunct to any type of resection of the colon. It prevents distension, moderates peristalsis, and promotes a smooth convalescence. It is useful as the first stage of a graded operation for radical removal of rectal cancer. Blind caecostomy for acute intestinal obstruction localized to the large bowel is useful, and often a life-saving operation. Complete by-passage of the faecal current by bringing out a loop of the caecum or right colon is superior as a means of decompression and irrigation before resection. For complementary caecostomy, however, when relief of distension by gas is the most important factor, a wing-catheter introduced into the caecum by Witzel's technique is very satisfactory.

Rankin, F. W. (1939) *Ann. Surg.* **110**, 380

CONCUSSION AND COMPRESSION

See also B.E.M.P., Vol. III, p. 355, Cumulative Supplement, Key No. 255, Surveys and Abstracts 1939, p. 289, and p. 70 of this volume.

The Concussional and Post-Concussional Syndromes

C. T. Van Valkenburg described the lymphopenia which is found after concussion. Together with unconsciousness and retrograde amnesia he regards it as a cardinal sign of concussion. In concussion the ventricular fluid, especially in the region of the third ventricle, is upset. This leads to disturbance in the hypothalamic region, which is known to bring about cellular and chemical changes in the blood. After the patient has regained consciousness the lymphopenia is the first sign to disappear. The patient may, however, be left with a variety of symptoms constituting the post-concussional state. These include giddiness, impairment of memory, and emotional instability. They are due to impairment of automatic functions and to the primary injury to the brain.

Van Valkenburg, C. T. (1940) *Lancet* **1**, 1003

CONJUNCTIVA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 365, Cumulative Supplement, Key No. 256, and Surveys and Abstracts 1939, pp. 128 and 289.

Inflammation due to Bacterial Infection

Gonococcal Ophthalmia

Sulphamylamide therapy.—F. A. Barbour and H. A. Towsley reported the results of 15 cases of gonorrhoeal ophthalmia treated with sulphamylamide and compared them with 15 consecutive cases before sulphamylamide was used. Sulphamylamide was given by mouth in these cases, except to 1 infant where it was given subcutaneously. The patients also received frequent irrigation and instillation of antiseptic solutions. Atropine was given if corneal complications threatened. Foreign protein injections and the instillation of silver nitrate were employed in some cases. Fifty-five cases treated by other authors were also summarized. They found that the incidence of corneal complications and the stay in hospital were reduced. Only mild toxic symptoms were produced in this series except in 1 case in which cyanosis was so extreme that the drug had to be withdrawn. The average daily dose of the drug in the first 3 days was 2.0 grains per pound for those under 1 year of age, and 1.0 grains for those over 1 year. It was found that large doses are necessary in infants to maintain an effective level in the blood, and they tolerate it very well.

W. J. Rein and O. B. Tibbetts employed local irrigations of sulphanilamide in 15 cases of gonococcal ophthalmia. The affected eye, or eyes, were irrigated every 15 minutes night and day with an 0.5 per cent solution of sulphanilamide in physiological saline. In cases with other gonorrhoeal complications, such as urethritis, a supplementary dose of sulphanilamide, 30 to 60 grains, by mouth was given. At the end of 24 hours a remarkable change generally occurred. The cornea became cleaner and brighter, secretion of pus almost ceased, oedema of the lids rapidly receded, and, in cases complicated by corneal ulcer, the lesion advanced no further or began to heal. Smears from the conjunctival sac were taken daily, and the patient was discharged when 3 consecutive daily smears showed the absence of intra- or extra-cellular diplococci. The average period necessary to obtain a negative smear was, by previous methods of treatment, 27.2 days, and by sulphanilamide irrigation 6.8 days. There were no ocular complications, and no relapses.

Conjunctivitis Due to Koch-Weeks Bacillus

Treatment with sulphonamide compounds --J. S. Guyton, investigating the effects of sulphanilamide and sulphapyridine on the growth of two strains of the Koch-Weeks bacillus (*H. influenzae*) in blood broth cultures, found that both drugs may exert an inhibitory or a bactericidal effect. Sulphapyridine in therapeutic concentrations (1 to 10 mg. per 100 c.c.m.) exerts a much greater effect than sulphanilamide in like concentrations. Conversely, in concentrations of 50 mg. per 100 c.c.m., sulphanilamide appears to be much more effective than sulphapyridine. The oral administration of sulphanilamide to 2 patients, and of sulphapyridine to 1, with ocular infections due to *H. influenzae* gave significant therapeutic results. The local use of an ointment containing 5 per cent sulphanilamide gave no beneficial results.

Streptococcal Pseudomembranous Conjunctivitis

Treatment with sulphanilamide --K. C. Swan and J. H. Allen employed sulphanilamide in 3 cases of streptococcal pseudomembranous conjunctivitis. The drug was given orally in a dosage of 1 grain per pound body weight, together with sodium bicarbonate. All 3 cases were serious infections which were progressing in spite of other forms of treatment. The first patient had lost an eye in a previous attack of the disease. Signs of clinical improvement occurred in all 3 cases after 2 to 3 days of treatment. There was a decrease in the amount of discharge, pseudomembranes did not reform after removal, and cultures did not reveal the presence of streptococci thereafter. The first patient had a mild recurrence of the disease 7 months after sulphanilamide therapy; this recurrence was controlled by further administration of the drug.

Barbour, F. A., and Towsley, H. A. (1939) *Arch. Ophthalm.*, N. Y., **22**, 581.

Guyton, J. S. (1940) *Arch. Ophthalm.*, N. Y., **23**, 1243.

Rein, W. J., and Tibbetts, O. B. (1929) *Amer. J. Ophthalm.*, **22**, 1126.

Swan, K. C., and Allen, J. H. (1939) *Amer. J. Ophthalm.*, **22**, 1255.

Tumours

Primary Carcinoma of the Limbus

F. P. Grenier reports a case in a man, aged 72, when treated by radium for a primary squamous-celled carcinoma, established by biopsy, of the limbus, which 5 years later had not recurred. From a review of the subject it appears that out of 18 recorded cases 14 patients were over the age of 50, and that the sex incidence was equal. Differential diagnosis should be made from (i) pinguecula and (ii) pterygium; in both of which carcinoma may supervene, otherwise a mistake cannot be made; (iii) a papilloma covering the cornea is less easy to diagnose; (iv) a congenital cyst of the cornea and a lipodermoid; (v) a dermo-epithelioma (a cystic or benign epithelioma) which never recurs or metastasizes; and (vi) xeroderma pigmentosum, on which a carcinoma may supervene. In a primary carcinoma surgical intervention should not go further than biopsy, as X-rays or radium gives better results.

Grenier, F. P. (1940) *Canad. med. Ass. J.*, **42**, 428.

CONVULSIONS IN INFANCY AND CHILDHOOD

See also B E M P., Vol III, p. 406 and Surveys and Abstracts 1939, p. 291

Aetiology and Treatment

M. G. Peterman reviewed 1,000 cases of convulsions in childhood. The majority of the cases, 34 per cent, were due to acute infection, 23.6 per cent were due to idiopathic epilepsy, and 15.5 per cent to cerebral birth injury. In the newborn to 1 month age group, 7.9 per cent of the total, 54 per cent were due to cerebral birth injury. Acute infection accounted for most of the cases in the 1 to 6 months and 6 to 36 months groups. Byers and Hass found cerebral venous sinus thrombosis in 50 infants who had suffered from convulsions associated with gastro-enteritis. The commonest cause of convulsions in older children, from 3 to 1½ years, was idiopathic epilepsy. Peterman emphasized that teething, worms, and adhesions of the foreskin or clitoris do not produce convulsions although delayed dentition may be associated with spasmodophilia of tetany. Peterman recommended cold sponging and a hypertonic enema as the immediate treatment of the convulsion. Spinal puncture should be done whenever facilities permit, whether the fluid is under pressure or not. The inhalation of chloroform is recommended, particularly in continuous convulsions. This can be followed by a sedative such as chloral hydrate. Morphine should not be used as it is too depressing to respiration and peristalsis. The child should rest in bed for some days after a fit, as it always produces cerebral injury. For recurrent fits phenobarbitone is the treatment of choice, and for idiopathic epilepsy a ketogenic diet is the best treatment.

Byers, R. K., and Hass, G. M. (1933) *Amer. J. Dis. Child.*, **45**, 1161.

Peterman, M. G. (1939) *J. Amer. med. Ass.*, **113**, 194.

CORNEA, INJURIES AND DISEASES

See also B E M P., Vol III, p. 424, Cumulative Supplement, Key No. 260, and Surveys and Abstracts 1939, pp. 128 and 292.

Injuries

From Broken Spectacle Glass

W. D. Horner reported 4 cases of penetrating wounds of the globe of the eye from broken spectacle glass. While, in view of the great number of people who wear glasses, injuries from broken glasses are remarkably uncommon, such injuries can be very serious. In 4 cases of serious injury to one eye reported, only 1 patient escaped with useful vision. All the patients received injections of foreign protein soon after the injury, and in only one did blood-staining of the cornea develop. In no case did panophthalmitis occur. In 3 of the cases rimless glasses were worn. X-ray examination to determine whether any piece of glass is retained is very important, most spectacle glass being radio-opaque.

Horner, W. D. (1939) *Arch. Ophthalm., N.Y.*, **22**, 439.

Ulcer

Treatment

Sulphanilamide — J. H. Bailey and I. Saskin reported 6 cases of severe corneal ulcer successfully treated with sulphanilamide. Four of the cases were the result of severe burns or trauma. In all cases the patients were relieved of their pain long before the ulcers were healed, and the progress of healing was more rapid than usual with other treatments. Once the condition is under control it is unnecessary to go on with the treatment. The final visual acuity in these cases was very good. In this series there were some toxic effects from the drug, such as dizziness, anorexia, and slight cyanosis. There was little interference with the continuation of the treatment. The drug was given orally in all cases, the dosage for a patient of 70 kg being 1 g. every 4 hours for the first day, 5 g. divided into 6 equal doses the second day; 5 g. the third day; 4 g. the fourth day, and 3 g. daily for the rest of the week. In some cases the drug may be continued in smaller doses for some days longer.

Bailey, J. H., and Saskin, E. (1939) *Arch. Ophthalm., N.Y.*, **22**, 89.

Symptomatic Affections

Interstitial Keratitis

Sensitivity to foods—A. M. Dean *et al.* report 6 cases of interstitial keratitis caused by sensitivity to certain foods. In some of the cases more than one article of food produced the symptoms. The disease begins with redness, discomfort and lacrimation in the eye. This is followed by haziness of the cornea and impaired vision. Severe pain occurs later and in one case was unbearable. Clinically the disease resembles syphilitic interstitial keratitis except that the vessels are less numerous and the 'salmon patch' is absent. Ulceration is rare and no intra-ocular complications occurred in this series. The treatment is specific. After removal of the offending food from the diet the symptoms and signs gradually regress. The following foods were incriminated in these patients: wheat, white of egg, and cheese.

Corneal transplantation—F. O'G. Kirwan reports a case of successful transplantation of the cornea in a case of opaque cornea from interstitial keratitis in which the eye was almost blind. The graft was taken from an eye blind from iridocyclitis and glaucoma, the cornea being perfectly clear. The graft was fixed with fine silk sutures which were removed on the fifth day, and remained perfectly clear throughout. Vision 2 months after operation was 6/6. It is stated that the operation was always justified in suitable cases as the results were often good. It was unnecessary for the donor to be of the same blood group as the recipient, and corneae from eyes blind from glaucoma furnished good grafts.

Rosacea Keratitis

Riboflavin therapy—I. V. Johnson and R. E. Eckardt discussed the treatment of rosacea keratitis, and other conditions in which the cornea is vascularized, with riboflavin. Thirty-six patients, 9 of whom also had cutaneous rosacea, were treated with riboflavin by mouth. Other skin diseases such as acne vulgaris were present in many of the other patients. The corneal ulceration in keratitis rosacea is similar to that produced in rats by a lack of riboflavin in the diet. The most effective method of giving riboflavin in this series was found to be as a sterile solution, each 5 c.c. containing 1.5 mg. of natural riboflavin, 1 to 3 times daily intravenously. The corneal lesions healed in 32 of the patients during treatment. Of the 9 patients with cutaneous rosacea, 4 showed satisfactory improvement. All the patients had been on a previous diet deficient in riboflavin or a lack of digestive secretions, notably hydrochloric acid. It is necessary to give riboflavin constantly to maintain the healing of the cornea.

Necrotic Keratitis

H. Eggers reported a case of necrotic keratitis (scleritis necroticans or scleromalacia perforans) associated with rheumatoid arthritis. This was a woman, aged 37, who was admitted to hospital with painful swollen joints, increasing loss of weight, and weakness. Both eyeballs had been painful and congested for several months. A diagnosis of rheumatoid arthritis was made. On examination of the eyes marked bilateral conjunctival and episcleral congestion were found. Gradually, within the next 3 weeks, 3 comparatively large swellings—2 in the right eye and 1 in the left—appeared beneath the cornea, and apparently in the sclera. Each swelling consisted of from 1 to 3 yellowish nodules. The swellings were limited to the upper anterior portion of the sclera, and ranged in area from about one-fourth to one-half of the corneal area. The congestion of both the superficial and deep blood-vessels became maximal and remained so. One month after admission a biopsy on the largest of the nodules evacuated several drops of moderately viscous yellowish-brown liquid. Fragments of the outer wall of the nodule were excised for histological examination. The inner wall of the cavity was formed of thinned-out sclera, thus proving that the nodules were intrascleral abscesses. The nodule, which was incised and drained, formed again. Later, all vision was lost as the result of massive bilateral haemorrhages in the vitreous. Shortly before the patient's death, sclerosing keratitis developed in the right cornea.

Dean, A. M., Dean, I. W., and McCutchan, G. R. (1940) *Arch. Ophthalmol.*, N.Y., **23**, 48.

Eggers, H. (1940) *Arch. Ophthalmol.*, N.Y., **23**, 501.

Johnson, I. V., and Eckardt, R. E. (1940) *Arch. Ophthalmol.*, N.Y., **23**, 899.

Kirwan, F. O'G. (1939) *Arch. Ophthalmol.*, N.Y., **22**, 21.

CRANIAL NERVE AFFECTIONS

See also B.E.M.P., Vol. III, p. 470; and Surveys and Abstracts 1939, pp. 86 and 294

The Seventh Nerve

Abnormal facial movements following injury.—E. P. Fowler writes on the abnormal facial movements that may follow injury of the seventh cranial nerve. They sometimes complicate facial paralysis of toxic origin. Tic-like movements and facial spasms are due to splitting of axons in the neuroma, several parts of the face being supplied by neurofibrils from one axon. The movements are therefore peripheral, not central, in origin and it is important to treat peripheral damage to the nerve as soon as possible in order to prevent serious damage and the occurrence of the movements.

Fowler, E. P., *Int. (1939) J. Amer. med. Ass.*, **113**, 1003

CYSTICERCOSIS

See also B.L.M.P., Vol. III, p. 523

Clinical Picture*Occurrence of Epilepsy*

F. D. W. Greig reports a case of a man, aged 52, who, when in China in 1923 became infected with tapeworm, probably *T. solium*. In 1924 he had an epileptic fit of the Jacksonian type affecting particularly the left arm. Up to the time of the report similar attacks had occurred, their severity lessening. Ictically had been occurring every 20 days. X-ray examination revealed no trace of cysticerci in the brain tissue, but this may have been due to calcification not being sufficiently dense to show radiologically. Calcified cysticerci were, however, shown in the soft tissues of the pelvis, abdomen, arms, and thighs. Although treatment is only palliative, diagnosis is important as it removes the fear of heredity attached to epilepsy, and avoids useless intracranial operations.

Greig, F. D. W. (1940) *J. trop. Med. (Hyg.)*, **43**, 49

DEAFNESS

See also B.L.M.P., Vol. III, p. 555, Cumulative Supplement, Key No. 284, and Surveys and Abstracts 1939, pp. 87, 100, and 296.

Otosclerosis*Treatment*

Methylene blue and sodium ricinoleate.—M. A. Corone reported on the treatment of otosclerosis by intrameatal injections of methylene blue and sodium ricinoleate, which, in some cases, counteracted further degeneration, and prevented the formation of further adhesions and exudations which contribute to the deafness. In the author's series 10 per cent sodium ricinoleate with ephedrine gave the best results. Tubal obstruction is often resistant to this treatment.

Oestrogenic substance.—J. Bernstein and L. Gillis stated that otosclerosis is probably related to some hormonal imbalance because it is familial and hereditary, is commoner in females than in males, often begins at puberty and ceases at the menopause, and is made worse by each pregnancy. They treated 18 males and 38 females with homogenic and heterogenic hormones. The type of hormone was changed from time to time without the patients' knowledge. Six cases were reported in detail, the female hormone used in these cases being oestron and the male perandren (testosterone propionate). Of the 58 cases 24 women and 7 men were improved by the treatment. In most cases the heterogenic hormone gave the best results.

Bernstein, J., and Gillis, L. (1939) *Lancet*, **2**, 1368

Corone, M. A. (1939) *Scalpel, Liège*, **92**, 896

Conduction Deafness*Prophylactic Treatment*

Oestrogenic substances and vitamins—G Selfridge claimed that oestrogenic substances probably play an important part in conduction-deafness. In many cases the administration of oestrogen completely relieves the tinnitus, menstrual irregularities, and other symptoms occurring during menstruation, but these symptoms generally recur when oestrogen is discontinued. It appeared that neither nerve nor conduction deafness is caused by any single factor, but seems to be linked with the various factors related to growth, such as the endocrine glands, vitamins, mineral salts, and amino-acids. The available evidence points to nutritional deficiencies, probably having their origin during pregnancy. An important factor in the prevention of deafness is an optimal diet containing all the essential food factors during pregnancy, and the maintenance of an adequate dietary throughout babyhood, childhood, and adolescence. The addition of aneurine hydrochloride (vitamin B₁), nicotinic acid, and other vitamins is often very helpful.

Selfridge, G. (1940) *Ann. Otol., etc., St. Louis*, **49**, 52

Deafness Generally*Treatment*

Surgical—W Hughson discusses the surgical treatment of all forms of deafness. As a first step in all cases, a complete toilet of possible septic foci is recommended, not as treatment but to prevent further progress of the disease. In addition, systemic causes of deafness must be excluded. Inflation and the passage of bougies are usually futile and to persist in them when they have failed helps to produce psychological depression. Before operation is undertaken, the tympanic membranes and Eustachian tubes must be shown to be normal and audiometer tests made. The maximal gain in the critical frequency range after operation is 25 decibels, therefore a loss of more than 50 decibels contra-indicates operation. The loudness balance between the two ears is equally important. Fatigue does not develop in a deaf ear with a purely conductive, as opposed to a purely neural, lesion. Lastly, intelligibility must be estimated, as post-operative improvements in this are the only valid proof of success.

Fistulization of the semicircular canals has a most beneficial immediate effect on hearing. The rationale for this is not known. Fistulization of the promontory does not give comparable results. The fistula must remain open. Though the results of this operation are dramatic it is technically difficult. On the other hand, fixation of the membrane of the round window with a tissue graft is relatively simple. The effect, however, is slow, though at its best it rivals fistulization. Before operation, if an unusual audiogram is obtained, an exploratory myringotomy is called for. This may show abnormalities on the surface of the promontory. Section of the tensor tympani muscle is entirely disappointing, as also is the division of adhesions, which promptly reform.

Hughson, W. (1939) *Arch. Otolaryng., Chicago*, **30**, 497

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

See also B1 M.P., Vol. III, p. 596, Cumulative Supplement, Key No. 288, and Surveys and Abstracts 1939, p. 298.

Effect of Vitamin Therapy on Incidence

Jundell and J. Billing reported on their investigations of the effect of antirachitic and antiscorbutic therapy on the incidence of dental caries. Two groups of children were observed over a period of 10 years. The first, which comprised 135 children, were given substances containing vitamin D and vitamin C from birth until the age of 2 years, thereafter 57 members of this group received no further treatment, while the remainder continued the treatment in a modified form until they had reached the age of 7½ to 8½ years. Wherever possible the infants in this group were breast-fed, and after the age of 9 months they received an adequate mixed dietary. Careful control of the dietary and of the home circumstances was

maintained during the whole period covered by the investigation. A second group of 113 children whose dietary was similar, except that no extra supply of vitamins was added, was also observed over the same period of time. As a result of this investigation the authors concluded that the antirachitic and antiscorbutic treatment had no influence whatever on the incidence of dental caries.

Jundell, I., and Billing, J. (1939) *Acta paediatr. Stockh.*, **23**, 295

Causes of Healthy Teeth

H. G. Miller and D. M. R. Crombie investigated the causes of healthy teeth in 25 children showing no caries. The children were between the ages of 10 and 14 years and a similar group showing caries were taken and studied as controls. It was found that the factors apparently associated with healthy teeth were a good family dental history and good general hygiene and diet. Breast-feeding was found to favour the incidence of good teeth and the most important factor was the absence of severe illness or an infectious fever at an early age. The absence of oral hygiene did not appear to affect the formation of good teeth.

Miller, H. G., and Crombie, D. M. R. (1939) *Lancet*, **2**, 131

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FIRED ERUPTIONS

See also B. I. M. P., Vol. III, p. 609, and Surveys and Abstracts 1939, p. 299

Toxic Dermatitis

Aetiology

Amidopyrine.—J. A. Buchanan reported a case of multiple symmetrical gangrene occurring during the prolonged administration of amidopyrine for chronic non-specific arthritis. The dosage of the drug was 5 grains, 4 times a day, together with 50 mg. of ascorbic acid, 3 times a day. About 2 months later the legs suddenly became swollen from the knees to the ankles, and bluish spots appeared on the thighs after a period of pain. The temperature rose to 103° F. The colour of the lesions steadily changed from blue to black, and became very hard. These areas of necrosis became loosened at the edges. On removal of the necrotic tissue, the muscles were exposed. The patient died several weeks after onset of the necrosis.

Sulphonamide compounds.—D. Fiskine reported 36 cases of sulphonamide dermatitis, seen chiefly at Guy's Hospital, London. Most of the cases showed a generalized morbilliform eruption, but urticarial, scarlatiniform, and light-sensitization rashes were also seen. The rashes mostly appeared between the eighth and tenth days of treatment and seemed to depend more upon the length of time the drug was given than upon the dosage. In some of the cases the rash cleared up without stopping the drug. In others, when the drug was stopped and then started again after the interval, the rash might appear again or in some cases no rash appeared. The skin eruptions were accompanied by malaise, irritation, and often pyrexia of 3° to 4°. It is necessary to diagnose the rash from such conditions as measles and scarlet fever. A history of taking the tablets and examination of the urine will help here. Intradermal skin tests are not of much use. Treatment should consist of stopping the drug and giving large quantities of fluids and alkaline diuretics to eliminate it. Ephedrene may be given to control the irritation and calamine lotion is a soothing local application.

Thiocyanates.—M. F. Green and J. S. Snow stated that thiocyanates, used to lower blood pressure, frequently give rise to toxic effects. They reviewed the literature of dermatitis arising from the use of this drug and reported a case. The patient received 0.32 g. of potassium thiocyanate twice a day and, on the eighth day of treatment, developed a pruritic eruption of the skin, beginning on the posterior aspect of the body. The next day large urticarial wheals appeared on the trunk, arms, and lower part of the legs. The temperature was 100.2° F. and the conjunctivae were injected. The treatment was stopped, but the condition persisted, reaching its height on the fourth day. The mucous membrane of the nose and throat also became oedematous and asthmatic attacks developed. Anorexia and weakness

also occurred and the condition did not begin to subside until about a week after the onset. The thiocyanate concentration in the blood fell slowly and, after 3 weeks, pigmentation and scaling of the skin still persisted. The patient was treated with a good fluid intake, bland lotions, and cool spongings. Adrenaline was given as nose drops for the oedema of the mucous membrane and hypodermically for the asthma. The reaction occurred when the blood thiocyanate level was lower than is usual in toxæmia. The patient had a history of allergic phenomena and it was therefore concluded that the condition was due to allergy arising in a patient with an idiosyncrasy for the drug.

Triethanolamine—G. H. Curtis and E. W. Netherton reported 2 cases of cutaneous hypersensitiveness to triethanolamine, a substance which is extensively used in the manufacture of cosmetics and in dermatological therapy. In one case, a man of 45, there was dermatitis of the face, neck, and upper part of the chest of one week's duration. The dermatitis had appeared suddenly, and was accompanied by burning and itching. The skin was red, swollen, and showed much weeping, crusting, and vesiculation. Patch tests with a shaving cream showed a strong positive reaction, and it was found that the cream contained triethanolamine. The other case, a woman of 41, developed a similar dermatitis after using an ointment containing the chemical. Patch tests with triethanolamine on many other individuals indicated that hypersensitiveness to it is rare.

9-bromo-fluorine—A. Cavendish describes a case of dermatitis from 9-bromo-fluorine, and a peculiar reaction to a patch test. This was a man of 22, a student of chemistry, who was carrying out research work involving the use of 9-bromo-fluorine. The eruption occurred on the face and later spread to the forearms, trunk, and lower limbs. The outstanding feature of the eruption was its striking intensity. It consisted of macules or very slightly raised discoid papules, of an intense purplish colour which faded on pressure, varying from a few millimetres to 1 inch in diameter. By their confluence they formed extensive irregular sheets containing islands of normal skin. The patient's reaction to a patch test with 9-bromo-fluorine had no obvious resemblance to the original eruption, and was such as might have been caused by the application of a local irritant.

Phenothiazine—F. DeFds *et al* pointed out that phenothiazine, an organic insecticide, has given rise to cutaneous reactions, consisting of intense itching, irritation, and reddening, sometimes accompanied by oedema, in gardeners and orchard-workers. These reactions have been variously diagnosed as sunburn, chemical burn, and dermatitis. The authors suggested that it is due to photosensitization, and not to local irritation by the substance. Oral administration of phenothiazine results in the excretion of the reversible oxidation-reduction system thionol-leucothionol. The latter is photosensitive, and, under anaerobic conditions, is oxidized to thionol when exposed to sunlight.

Dermatitis due to dyed clothing—I. Epstein discussed 8 cases of dermatitis due to dyed clothing. Dyed fabrics may cause dermatitis venenata, photosensitivity, pyoderma, hidradenitis suppurativa, lichen simplex chronicus, and urticaria. One of the most important factors in the production of dye dermatitis is hyperidrosis. Most of the offending dyes have been shown to be water-soluble. Perspiration probably plays an important part in causing these dermatoses by dissolving the dye from the cloth. Most writers stress the frequency of dye dermatitis in women. In the author's cases approximately 76 per cent occurred in men. It is doubtful therefore if sex or the menopause is of any significance in the development of sensitivity to dyes.

Cosmetics.—G. L. Wolcott reviewed selected literature on the composition and dangers of imported cosmetics. While adequate statistics are lacking, the incidence of severe injury from the use of cosmetics is relatively low in comparison with the number and variety employed. Farlier cosmetics often resulted in severe systemic poisoning from lead, mercury, etc.; nowadays most cases of injury belong to the class of allergic dermatoses. The most serious offenders are the aniline dyes and coal-tar derivatives. Of all cosmetics hair dyes are the worst offenders, in 111 cases of injury due to hair dye, such dangerous ingredients as lead acetate, sulphur, pyrogallol and *para*-phenylenediamine were found. Eye-lash darkeners are particularly harmful; such products either coat the lashes with mascara or lamp-black, or actually stain them; necrosis of the cornea has been reported from their

use. Toilet powders may cause harm on account of impurities such as lead, bismuth, arsenic, and mercury. Allergic reactions may occur on account of certain ingredients such as orris. Nail polishes are relatively innocuous, although they frequently cause minor disturbances of the nails, for example brittleness and splitting. Synthetic perfumes have given rise to many dermatoses; an important feature of many cases is the appearance of a curious photo-pigmentation.

Cosmetic eye—L. P. Ereaux describes under the above title a disfiguring dermatitis involving the eyelids, of 2 kinds: (i) in which the ocular tissues are affected as part of a more widespread facial inflammation, for example, from rouge burns, (ii) in which the eyelids alone suffer. The earliest sign in these cases is an acute inflammatory reaction to the irritant; later, the eyelids come to resemble those of an aged person, the skin becoming scaly, thickened, and pigmented. In facial dermatoses the eyelids tend to be affected early and to be the last to recover. The sufferers are nearly all women, many of them neurotic. The possible causes of this peri-ocular dermatitis and the composition of the preparations are very numerous and often complex; reference is made to a lipstick with 51 constituents, and to one with a toxic content of cadmium and selenium. Cold creams may be irritating from the addition of essential oils, vanishing creams from the presence of glycerin, and a sunburn cream containing carbolic acid provokes dermatitis. Soaps may be responsible from various contents, and of all the expressed oils that of cacao is the most irritating of those used as saponifiable fats. Freckle removers exert an exfoliating action and are often harmful from the presence of mercury, bismuth, formaldehyde, salicylic acid, zinc sulphocarbolate; and resorcinol. Hair dyes, eye-shadow preparations, eye drops, and eye-lash curlers are also dangerous. Nail cosmetics, because of the frequency of unconscious contact of the fingers with the eyelids should be borne in mind.

In the acute stage soothing applications only such as the old-fashioned starch poultice, warm or cold, compresses of ichthammol water 1 per cent and solution of aluminium acetate 0.5 per cent, should be used, or an oily calamine emulsion may be painted on with a fine, camel-hair brush, in the subacute phase 0.5 per cent each of sulphur and salicylic acid in an albolene base is helpful, and in the chronic cases X-rays, sub-fractional doses of unfiltered radiation, equivalent to 50 r every 5 days for 4 to 6 doses are recommended. Finally, patients should avoid the 7 Cs—cocktails, coffee, condiments, cigarettes, carbohydrates, chocolates, and cosmetics.

Mint.—W. M. Sams reports 2 cases of occupational dermatitis in bartenders due to contact with mint, which they employed in the preparation of drinks. Small deep-seated blisters associated with burning and itching occurred along the thumb and index fingers. The results of patch tests with materials they usually handled were negative, except with mint.

Buchanan, J. A. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 678.

Cavendish, A. (1940) *Brit. J. Derm.*, **52**, 155.

Curtis, G. H., and Netherton, I. W. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 729.

DeEds, F., Wilson, R. H., and Thomas, J. O. (1940) *J. Amer. med. Ass.*, **114**, 2095.

Lpstein, F. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 1044.

Ereaux, L. P. (1940) *Canad. med. Ass. J.*, **42**, 364.

Lrskine, D. (1939) *Brit. med. J.*, **2**, 104.

Green, M. E., and Snow, J. S. (1939) *Arch. intern. Med.*, **64**, 579.

Sams, W. M. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 503.

Wolcott, G. L. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 64.

Collier's Stripes

F. R. Bettley discusses collier's stripes, a common dermatosis among coal-miners, and consisting in the presence on exposed parts of the skin of numerous linear and irregularly-shaped marks, the result of scratches and small injuries which have healed without scar-formation, and in which coal-dust has been deposited before healing has been complete. They are most numerous on the face, forearms, and hands, are commonly linear or angular in shape, and up to 1 inch or so in length. They are light greyish-blue in colour, generally a little fainter than that of the

indian-ink tattoo Various authorities have stated that small wounds sustained by coal-miners rarely suppurate, and that the coal particles lie in the tissues without exciting the slightest reaction The author disagreed with this; suppuration is no more and no less common with these wounds than with similar wounds sustained by other people, or by coal-miners themselves in other circumstances The coal-dust does not seem to prevent suppuration On histological examination particles of coal-dust of all sizes up to 100μ are found at all depths in the dermis They tend to be grouped, particularly in the vicinity of vessels They are for the most part enclosed in multinuclear giant cells of the foreign-body type, and surrounded by a collection of fibrocytes and fixed-tissue cells, giving the appearance of fibrous nodules (see Plate I) In Indian-ink tattooing, on the other hand, the particles are always less than 1μ , the cellular reaction is less, and giant cells are not found

Bettley, F. R. (1940) *Brit. J. Derm.*, **52**, 129

Prevention of Industrial Dermatitis

J. V. Klander *et al.* investigated the question of prevention of industrial dermatitis. They emphasized the importance of mechanical devices in the prevention of industrial dermatitis, and the need for education of workmen and others concerned in preventive measures, especially in the care of the skin, and in harmless methods of cleansing it. They stated that a 10 to 30 per cent solution of sodium hyposulphite and a 0.5 per cent solution of sodium metasilicate are harmless agents for removing such substances as paint, ink, and dye, and as general cleansers. A formula consisting of a mixture of equal parts of sulphonated neat's foot oil and liquid paraffin, and white granulated corn meal was advocated as a substitute for mechanical abrasive soap. 1 part by weight of the mixed oils is added to $1\frac{1}{2}$ parts by weight of the corn meal. To prevent growth of mould or bacteria 0.5 per cent solution of chlorbutol is added.

Klander, J. V., Gross, F. R., and Brown, H. (1940) *Arch. Derm. Syph.*, **N.Y.**, **41**, 331

DERMATITIS, EXFOLIATIVE

See also B.I.M.P., Vol. III, p. 619.

Von Ritter's Disease

Treatment

Sulphapyridine—N. W. Ryan and L. Goldman record a case in a female infant, aged 4 weeks, who when 3 weeks old came under observation with gastro-intestinal symptoms and a week later showed the rare condition described by Ritter von Rittershausen, and also called dermatitis exfoliativa neonatorum and regarded as a variant of pemphigus neonatorum. The Wassermann reaction was negative and syphilis was considered to be eliminated. Recovery followed treatment with daily transfusions of 50 c.cm. of blood, an initial dose of 6 grains of sulphapyridine, then 2 grains every 4 hours for the first 3 days, and for 4 days more 1 grain of sulphapyridine. Recovery was by this time rapid and treatment was discontinued. The disease occurs in infancy, may be sporadic, as in this case, or epidemic, and is characterized by rapidly spreading redness, vesicles and bullae, epidermolysis and exfoliation. A mortality of 50 per cent or more has been observed. Three other cases seen by the authors all proved fatal.

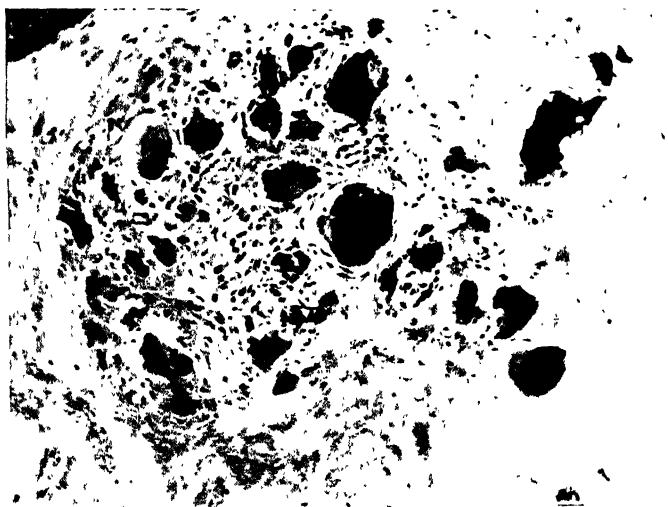
Ryan, N. W., and Goldman, L. (1940) *Amer. J. Dis. Child.*, **59**, 1057.

DERMATOSES, PYOGENIC

Treatment

Sulphanilamide

A. Strickler and M. J. Stone employed sulphanilamide in dermatoses. Two cases of impetigo contagiosa neonatorum were successfully treated. Eight cases of secondary pyogenic dermatoses were reported. The pyogenic lesions supervened on existing disease such as eczema. Treatment of the eczema was necessary in order to



A collection of coal particles contained in giant cells and surrounded by fibrocytes and fixed-tissue cells 140 (*From British Journal of Dermatology and Syphilis*, 1940)

PLATE I

(Continued on page 200)

treat the pyoderma. Sulphanilamide was of value in these cases by reducing this period and in giving the skin a rest from local antiseptic application. Four cases of sycosis vulgaris were also treated with sulphanilamide. Two patients improved markedly and in the other 2 the skin became quite clear. Strickler and Stone concluded that sulphanilamide was unnecessary in the milder forms of pyoderma but was very useful in those that might be fatal or in rapidly spreading and chronic types.

Strickler, A., and Stone, M. J. (1939) *Arch. Derm. Syph. N.Y.*, **40**, 244

DERMOID CYSTS

See also B.E.M.P., Vol. III, p. 635.

Intradiploic Epidermoids

J. G. Love and A. A. Bailey report complete and successful removal of an intradiploic epidermoid tumour from a man, aged 46, with a history of intermittent throbbing headache for 14 years, and subsequently other symptoms, including deafness and tinnitus for 13 years, and mild psychiatric phenomena. Radiologically the left half of the occipital bone was much thinned and the diploe expanded, the margins of the affected area being sharply defined. These changes pointed to the presence of a large tumour, such as an epidermoid or cholesteatoma. There was secondary erosion of the sella turcica and the floor of the anterior fossa due to the pressure of the tumour. The tumour, which weighed 200 g., and when exposed presented the typical silvery sheen of an epidermoid, showed microscopically squamous epithelium. The patient's father had died of a brain tumour, the nature of which was not known. In a review of these congenital tumours a division is adopted into (i) intradural and (ii) extradural, also intradiploic. Intracranial epidermoids are rare, and intradiploic rarer than intradural. The intradiploic epidermoids grow slowly and symptoms seldom appear before adult life. Palpation of the cranium does not show evidence of any mass or even a disturbed contour of the skull unless the outer table is much eroded.

Love, J. G., and Bailey, A. A. (1940) *Proc. Mayo Clin.*, **15**, 129

DIABETES INSIPIDUS

See also B.E.M.P., Vol. III, p. 639; Cumulative Supplement, Key No. 295; and Surveys and Abstracts 1939, p. 301

Aetiology

Role of Pituitary

P. Heinbecker and H. L. White investigated the influence of the pituitary on water balance. There are two views about the causation of diabetes insipidus, (i) the hypothalamus is primarily involved and (ii) the pituitary is responsible. Heinbecker and White investigated both these hypotheses by experiments on more than 100 dogs. It was found to be necessary to remove or destroy the neural hypophysis, i.e. the pars nervosa, stalk, and median eminence, to produce diabetes insipidus. The anterior lobe is probably only concerned with diuresis. Although thyroid extract produced a diuresis in normal dogs it had no effect upon hypophysectomized ones unless anterior lobe extract was given as well, this supports the view that the thyroid acts under the direction of the pituitary. The effect of thyroidectomy on experimental diabetes insipidus depended upon how early in the condition it was performed, the earlier it was done the greater effect it had upon the polyuria. In one patient similar results were noted, complete thyroidectomy considerably reducing the polyuria in dogs, but creatinine clearance was normal. Deprivation of water for 24 hours showed that dogs with diabetes insipidus and hypophysectomized dogs without polyuria cannot concentrate urine so well as the normal animals. The dogs with diabetes insipidus were also far less tolerant of water deprivation than normal controls. In the hypophysectomized and diabetes insipidus dog there is a chronic deficiency of pitressin; their diuretic response to water by mouth, at any rate, during the first week or 10 days after operation, is normal. The lag in water output

behind water load is similar to that of the normal dog. This does not support Verney's contention that the lag represents the time necessary for prefrontal pituitary to disappear.

Division of Stalk of Hypophysis

W. I. Dandy reports a case of disseminated sclerosis in which, during exploratory operation of the brain, the stalk of the hypophysis was divided with scissors midway between the base of the brain and the diaphragm of the sella turcica without damage to the contiguous part. As a result, permanent polyuria and polydipsia ensued. There was no disturbance of the known hypophyseal functions, such as menstruation, pregnancy, lactation, weight, blood-pressure, sugar content of the urine. Division of the stalk of the hypophysis was regarded as solely responsible for polyuria and polydipsia.

Dandy, W. I. (1940) *J. Amer. med. Ass.*, **114**, 312.

Hembecker, P., and White, H. I. (1939) *Ann. Surg.*, **110**, 1037.

DIABETES MELLITUS

See also B. F. M. P., Vol. III, p. 644; and Surveys and Abstracts 1939, pp. 67 and 31.

Diabetic Coma

Prognosis

I. B. Owens and S. S. Rockwern discuss the prognosis, and analyse 92 cases of diabetic coma. They found that the prognosis depends on the amount and extent of damage done to the brain before treatment is started. Anoxia, rather than ketosis, was thought to contribute most to the brain damage. If the brain is therefore the mentality were not much affected the patients rarely died in coma. Emphasis is laid on the fact that true coma must be differentiated from the ketosis or 'pre-coma', the latter responding well to accepted methods of treatment. The combining power of the blood with CO_2 is of no value in estimating the prognosis in diabetic coma. Treatment with glucose, alkalis, or insulin does not reduce the mortality in unconscious patients. As diabetic coma specially occurs, it has a higher mortality, in females at puberty and the menopause, endocrine structures other than the pancreas are probably implicated in diabetes mellitus.

Owens, I. B., and Rockwern, S. S. (1939) *Amer. J. med. Sci.*, **198**, 252.

Diabetes in Children

Prognosis

With insulin treatment. A. E. Lykow observed that diabetes mellitus in children sometimes disappears completely if treated early with insulin. In one case diabetes mellitus appeared together with catarrhal jaundice and the diagnosis of diabetes was made on pancreatic deficiency. If this is corrected early by administration of insulin and careful dieting, diabetes need not recur in later life. The author believes in a prophylactic stimulation of the pancreas by insulin, if too great a stress is put upon it by faulty diet.

Lykow, A. (1939) *Kinderarztl. Prax.*, **10**, 402.

Clinical Picture

Houssay Phenomenon

J. H. Kotte and A. R. Vonderahe report a case of diabetes mellitus, which was complicated by an infarct in the anterior pituitary, and terminal hypoglycaemia. Houssay described the sensitivity of hypophysectomized animals to insulin and the virtual disappearance after hypophysectomy of the diabetes mellitus induced by depancreatization. The authors therefore describe this case as the Houssay phenomenon in man. The patient was a diabetic who for years had not received regular treatment. He took a diet of his own and was known to inject himself with insulin when the death arose. He suffered from a cough and weakness. About fortnight before death he complained of a pain in his head, became progressively weaker, almost stuporous, and finally died 18 hours after admission to hospital.

On admission his blood-pressure had been low, the temperature raised, and the urine free from sugar. The blood-sugar level was only 31 mg. per 100 c cm. Necropsy showed infarction of the anterior pituitary, acute ileitis, peritonitis, and pulmonary tuberculosis. The patient was, in effect, hypophysectomized and died of acute hypoglycaemia. The cause of the infarction was not determined.

Lesions of Legs

F. W. Williams and T. J. O'Kane discuss lesions of the legs in diabetes mellitus with a view to indicating the sites for amputation. Some lesions are vascular, some infective, and others mixed, arterial insufficiency being the most important. Purely vascular lesions are gangrenous from the start, whereas the purely infective are not associated with gangrene. The severe mixed cases are also initially gangrenous, becoming infected before demarcation has occurred. Some mixed cases start as infective and oedema produces secondary vascular obstruction. By a complete clinical examination, both general and local, the degree of vascular and infective elements in all cases can be accurately assessed. The great majority of purely vascular superficial lesions do well without operation. Extensive vascular lesions of the toe, which fail to demarcate, call for amputation in the calf or thigh. Purely infective lesions call for conservative treatment or careful local drainage. In the mixed lesions, the treatment depends entirely upon the amount of vascular involvement.

Xanthoma Diabeticum with Lipodystrophy

R. D. Lawrence reports the case of a woman, aged 26, with diabetes mellitus, xanthomatosis, persistent lipaemia, hypercholesterolaemia, extreme hepatosplenomegaly, lipodystrophy, enlarged and fibrotic lymphatic and parotid glands, and a basal metabolism persistently between -50 and -75. Splenic and hepatic puncture did not give any assistance. Parkes Weber had never seen such a syndrome of rare manifestations in diabetes mellitus, but suggested that the condition of the parotid glands, in which a biopsy suggested lymphocytic infiltration, should be compared with Sjögren's syndrome (Parkes Weber and Schluter).

Associated Glycogenic Hepatomegaly

N. B. Friedman reported 2 cases of diabetes mellitus in which glycogenic hepatomegaly was associated with insulin hypoglycaemia. In both cases the pancreas was small, or the islet tissue scanty. In the diabetic organism, in the presence of adequate dextrose, glycogen is stored in the liver under the influence of insulin, and this may have been the mechanism involved in these cases.

Associated Disturbance of Biliary Function

R. Rathery *et al.* discuss the coexistence of latent icterus and disturbances of biliary function in diabetes mellitus. Variations in the blood-sugar level are said to be responsible for bilirubinaemia, but the origin of biliary disturbances in diabetes mellitus is complex and due to more than one cause. Bilirubinaemia varies with the rise and fall of the sugar in the blood, and improvement of the glycaemia is accompanied by improvement in the biliary function. A van den Bergh test should be performed in the routine examination of diabetics and the coexistence of latent icterus should not be regarded as alarming.

Friedman, N. B. (1940) *Arch. Path.*, **29**, 415.

Kotte, J. H., and Vonderahe, A. R. (1940) *J. Amer. med. Ass.*, **114**, 950.

Lawrence, R. D. (1940) *Proc. R. Soc. Med.*, **33**, 329.

Rathery, F., Polydorides, J., and de Traverse, P. M. (1939) *Paris méd.*, **29**, 33.

Weber, F. P. (1940) *Proc. R. Soc. Med.*, **33**, 329.

— and Schluter, A. (1937) *Dtsch. Arch. klin. Med.*, **180**, 333.

Williams, F. W., and O'Kane, T. J. (1940) *Arch. Surg., Chicago*, **40**, 685.

Diagnosis

The One-Hour Two-Dose Dextrose Tolerance Test

M. W. Matthews *et al.* described the significance of the one-hour two-dose dextrose-tolerance test of Exton and Rose in the diagnosis of diabetes. They investi-

gated its effects on 117 normal people, 304 diabetics, and 70 persons suffering from renal glycosuria. The procedure consists of giving 100 g. of dextrose in 650 c.c. of water in 2 doses at 30-minute intervals. Urine and blood are collected after overnight fast and the first dose is then given; 30 minutes later a sample of blood again collected, then the second dose is given. After another 30 minutes a third sample of blood and a second of urine are collected. The results of the test show that, if the fasting blood-sugar exceeded 120 mg. per 100 c.c.m., diabetes was present. The fasting level was not above 110 mg. in any normal person. At the end of 1 hour those showing a level above 180 mg. per 100 c.c.m. were diagnosed as diabetic. Those above 158 mg. were diagnosed as presumptive diabetics. All those in whom the level was below 154 mg. were found to be normal. The older the patient the higher was the blood-sugar level at every estimation in this test. The author stated that the level at the end of the hour, when the readings given above were taken, is reliable for the diagnosis of diabetes and that the test is not invalidated if the other two blood-sugar estimations are omitted.

Intravenous Dextrose-Tolerance Test

R. F. Tunbridge and E. C. Allibone described an intravenous dextrose-tolerance test for use in cases of idiopathic glycosuria and steatorrhoea. Two methods may be used, the continuous administration of a weak solution, and the rapid injection of a more concentrated one. Tunbridge and Allibone injected 92 c.c.m. of a 30 per cent solution of dextrose in distilled water into the median basilic vein in 3 minutes. The injections were made between 9 and 11 a.m., most of the subjects having had nothing to eat since the previous day, 0.1 c.c.m. of blood was taken from the ear for analysis at intervals of $1\frac{1}{2}$ to $7\frac{1}{2}$ minutes for at least 60 minutes after the injection. Forty healthy medical students and 92 hospital patients were investigated. The blood-sugar curve returned to normal within 1 hour in all the healthy students. The precise time of the return to normal was constant in the individual on repeated tests, but varied in different students. Various factors alter the curve, but there was no constant reaction for any one factor. Thus age, the amount injected, diet, the presence of infection, etc., all had an effect upon it. After the injection, glycosuria occurred in all the urines examined. Liver disease was associated with impaired dextrose tolerance, but the decreased tolerance was no greater than that in patients suffering from other diseases in which the liver, so far as could be ascertained, was not involved.

Matthews, M. W., Magath, T. B., and Berkson, J. (1939) *J. Amer. med. Ass.* **113**, 1531.

Tunbridge, R. F., and Allibone, E. C. (1940) *Quart. J. Med.*, **9**, 11.

Treatment

Antidiabetogenic Effect of the Pituitary

In a preliminary report on an antidiabetogenic effect of a primary alcoholic extract of prime whole gland pituitary administered orally, J. B. Collip (1940), follows up his account (1940, a) of an orally active medullotrophic principle in primary extract of pituitary tissue. In the light of this observation and of the part played by the adrenals in metabolism it seemed advisable to determine the effect of the same extract, given by the mouth on patients with diabetes mellitus, upon normal rabbits, rats, and monkeys, and one de-pancreatized monkey. The extract contained the glycotrophic principle, but this is not effective in increasing glycogen stores unless given by injection to the test animal, the mouse; it is rich in the melanophore principle, and contains some corticotrophic substance. The on effects consistently following the oral administration of the extract are the medullary reaction in the adrenals of the hypophysectomized rat and the mild hypoglycaemic reactions seen in normal starved monkeys and rabbits, the latter effect, though fairly consistent, is not very striking and, indeed, might be disregarded by one familiar with the possible vagaries of blood-sugar curves. Protocols taken in 1935 and 1936 showed hypoglycaemic action due to some extracts even more striking than those now reported, but which at the time were discounted. The negative result in the de-pancreatized monkey suggests that the extract cannot act in the absence of the pancreas. The following questions are raised for further investigation.

tion: (i) What is the mechanism by which this extract taken orally affects carbohydrate metabolism; (ii) is the effect on carbohydrate metabolism due to the same substance which causes the medullary reaction in the adrenals of hypophysectomized rats; (iii) if so, is the effect on carbohydrate metabolism secondary to some form of activation of the adrenal medulla, or is it due to a direct action of the substance on the periphery; (iv) is there a true pancreatotrophic hormone, as has been claimed by Anselmino, Herold, and Hoffmann, and by Richardson and Young, and if so, is the effect upon carbohydrate metabolism of this extract due to direct activation of the islet tissue; (v) is there some type of synergistic action between some constituent of this extract and insulin; (vi) is the medullary reaction secondary to a primary pancreatotrophic action; and (vii) what is the relationship of the substance affecting carbohydrate metabolism to the diabetogenic substance effective by the injection of crude extracts containing it?

Insulin Suppositories

It is not usually possible to give insulin by mouth or rectally because it is destroyed by the digestive processes. B. Brahn (1940, a) made an insulin suppository in which the insulin was protected from these ferments by cocoa butter and the addition of a combination of lactic and palmitic acids. The addition of saponin increased the duration and intensity of the effect of the insulin. Tests were made on rabbits and healthy men and it was found that insulin given per rectum in these suppositories acted quickly and the action was over rather rapidly. The suppositories have been used clinically by other workers and Brahn considered that they are worthy of further tests in the treatment of diabetes.

Avitaminosis during Insulin Therapy

V. P. Sydenstricker *et al.* state that the glossitis and stomatitis occurring in patients with diabetes mellitus may be due to avitaminosis resulting from abnormal carbohydrate metabolism, and report 2 cases showing clinical signs of pellagra. The dietary of the patients was adequate in vitamins but the signs appeared when they received increased carbohydrates accompanied by increased insulin to control them. It is suggested that the increased insulin so increases the carbohydrate metabolism that coenzymes I and II, both of which contain nicotinic acid, are destroyed. The stores of this vitamin are therefore exhausted. Nicotinic acid relieved the symptoms until the insulin was increased, when they reappeared and nicotinic acid had to be given again. Exactly the same reaction was observed with riboflavin given intravenously.

Zinc-Protamine-Insulins

W. L. Lowrie and D. P. Foster studied the hypoglycaemic reactions in 89 patients who had received both regular and zinc-protamine-insulins for at least 6 months. They found that fewer reactions occurred with zinc-protamine-insulin than with regular insulin, and that reactions with the former were in general less severe and less frequent. Patients who were overweight were relatively free from reactions with zinc-protamine-insulin. The authors recommended the following plan for changing over a patient from regular insulin to zinc-protamine-insulin. On the first day zinc-protamine-insulin is given in a dosage four-fifths that of the total daily dose of regular insulin. In addition, if 3 daily doses of regular insulin have been given, the first 2 doses are given as usual, and half the third is given. On the second day the same dose of zinc-protamine-insulin is administered, and the full first dose of regular insulin, but the noon dose is halved and the last dose omitted. On the third day the same amount of zinc-protamine-insulin is given, the breakfast dose of regular insulin halved and the lunch and supper insulin omitted. On the fourth day zinc-protamine-insulin alone is given.

Allergy in relation to local reactions.—R. A. Kern and P. H. Langner investigated the nature of the local reactions at the site of injection of zinc-protamine-insulin. They obtained no positive sensitizing tests to protamine in 110 diabetic patients and so concluded that the reaction was not due to allergy. They suggested that the reaction might be due to injecting the drug into instead of beneath the skin, alcohol irritation when alcohol had been used to sterilize the syringe, or to infection due to

faulty asepsis. They reported 2 cases in which patients had received insulin, 1 of them for years, for the treatment of diabetes. They were put on to zinc-protamine-insulin, and 5 and 8 days later local reactions developed. It was supposed that insulin sensitivity developed in these cases because of the slower absorption of the antigen (insulin) from the zinc-protamine-insulin.

Protamine-Insulin and Zinc-Protamine-Insulin

A. Herzog and H. Hoernisch treated a large number of patients with protamine-insulin and protamine-zinc-insulin with the same good results as are obtained by others. They found, however, in some cases allergic reactions due to the protein contents of the preparation. They suspected that there might be formation of anti-protamine bodies in the blood. If this proved to be true, it would diminish the 'depot' effect of the zinc-protamine-insulin. Five patients received first insulin and, after a week, the same amount of zinc-protamine-insulin. The diet was standardized. The blood sugar level was estimated regularly and compared. The effect of protamine-insulin and zinc-protamine-insulin was diminished after a time. The blood sugar and glycosuria rose, after some time hypoglycaemia might result from the greater effect of the zinc-protamine-insulin (loss of 'depot' effect). It might be necessary to give the zinc-protamine-insulin in 2 daily injections instead of one.

Combined use of Zinc-Protamine-Insulin and Soluble Insulin

G. M. Wauchope investigated the interaction of zinc-protamine-insulin and soluble insulin when given in combined doses. Seventeen diabetic patients, who were balanced on a combined dose of zinc-protamine-insulin and soluble insulin and 5 active chronic diabetics were investigated. Two blood-sugar curves were taken in each case, one after separate injections of the 2 insulins and the other after injection of the 2 mixed in a syringe. It was found that combining the 2 insulins modified the action of soluble insulin, and that more of it had to be given to produce hypoglycaemia in the morning if it were mixed with the zinc-protamine-insulin. It was concluded that it is better to give the 2 insulins separately, or if from the same syringe they should not be allowed to mix.

Comparative Merits of Crystalline, Regular, and Zinc-Protamine-Insulins

A. Marble and I. Vartiainen compared the action of crystalline insulin with that of regular insulin and zinc-protamine-insulin. Eight patients with severe chronic diabetes mellitus and 8 normal persons were investigated. Rabbits were also tested for purposes of comparison. Both crystalline and amorphous insulin lowered the blood-sugar at the same rate in diabetic and normal persons. The two preparations also acted for the same length of time in both groups. The return to the normal level of blood-sugar took slightly longer when the crystalline type was used. The blood and urine sugar levels were slightly lower when crystalline insulin was used, but the difference was too small to be of clinical significance. Both these types of insulin, as well as the slowly-acting zinc-protamine-insulin, are useful in the treatment of diabetes.

Alum-Precipitated Insulin

L. Rosenthal *et al.* studied the effects of alum-precipitated insulin on 12 diabetics who required large amounts of insulin, up to 160 units per day. They found that the total dose could be given safely in one morning injection if given as alum-precipitated insulin. The drug began to act 2 hours after injection, and therefore supplementary injections of ordinary insulin were unnecessary. The effect was more evenly distributed over the 24 hours than in the case of protamine-zinc-insulin. Only 1 patient, who had had several previous attacks on the old insulin, developed hypoglycaemic tetany. The patient recovered quickly and subsequently took the same doses of alum-precipitated insulin with no untoward effects. The physical and mental health of all the patients improved and some gained weight. During the treatment some of the patients were able to receive a reduced dose and still maintain a steady equilibrium.

Protamine-Hexamine-Insulin

B Alpert employed a combination of hexamine-insulin and zinc-protamine-insulin, in cases of juvenile diabetes. The hexamine-insulin gives an immediate and some intermediate hypoglycaemic effect, while the delayed action of the zinc-protamine-insulin is preserved. When mixed in the same phial, the two insulins retain their individual characteristics. The author claimed that the use of this mixture eliminated the necessity for supplementary injections of insulin during the day in cases treated with zinc-protamine-insulin, so that the patient need have only one injection. In one case reported the patient was standardized on 25 units of zinc-protamine-insulin and 8 units of hexamine-insulin given in a single injection before breakfast, in another case a mixture of 80 units of zinc-protamine-insulin and 16 units of hexamine-insulin was given in a single daily injection.

Zinc-Globin Insulin

L. Bauman stated that zinc-protamine-insulin has the disadvantage that its slow continuous action may produce hypoglycaemic attacks when no carbohydrate is being taken, for example, during the night. Local reactions may also occur at the site of injection. He used zinc-globin insulin in water clear solution for adult and child diabetes over a period of 2 years. The preparation employed consisted of a mixture of 80 units of insulin per c.c.m. with native globin in the proportion of 1,000 units of insulin to 38 mg. of globin and 3 mg. of zinc chloride. Sixty units or more per day, 145 units being the biggest single dose, produced no harmful effects. Severe cases requiring 100 units or more a day were difficult to control satisfactorily for 24 hours, but some of them were better controlled than they had been with zinc-protamine-insulin. If the morning dose were too large, hypoglycaemic shocks occurred in the late afternoon rather than during the night. There were no skin reactions in this series.

'Dcurvion' Pectin-Insulin

B Brahn (1940, b) endeavoured to find a form of insulin with a prolonged action, but no depot effect. He wished to avoid the depot effect because insulin may be stored longer than is intended, and because it may be given off irregularly, leading to a sudden hypoglycaemia. He also tried to avoid zinc, as used in zinc-protamine-insulin, because it is not yet known how zinc given over a period of years will affect diabetics. Undesirable side-effects may be produced. After experimenting with many colloid and gelatinous substances he found that a 4 to 5 per cent solution of pectin of pH 4.0 to 4.4 was a suitable vehicle for the insulin. He named this solution 'dcurvion'. Injection of this insulin produced a steady prolonged absorption beginning immediately after injection. The effect did not last so long in rabbits as in man. In man the blood-sugar decreases for 3 hours after injection and does not rise again until after 6 hours. Because the insulin is soluble in the pectin this preparation may be given intravenously. When zinc was added to the solution it made no appreciable difference to these results.

Albert, B (1939) *Arch. Pediat.*, **56**, 647.

Anselmino, K. J., Herold, L., and Hoffmann, I. (1933) *Klin. Wschr.*, **12**, 1245.

Bauman, I. (1939) *Amer. J. med. Sci.*, **198**, 475.

Brahn, B. (1940, a) *Lancet*, **1**, 829.

— (1940, b) *ibid.*, **1**, 1078.

Collip, J. B. (1940, a) *Canad. med. Ass. J.*, **42**, 2.

— (1940, b), *ibid.*, **42**, 109.

Herzog, A., and Hocmisch, H. (1939) *Med. Klin.*, **35**, 908.

Kern, R. A., and Langner, P. H., Jnr. (1939) *J. Amer. med. Ass.*, **113**, 198.

Lowie, W. L., and Foster, D. P. (1940) *Amer. J. digest. Dis.*, **7**, 101.

Marble, A., and Vartiainen, I. (1939) *J. Amer. med. Ass.*, **113**, 1303.

Richardson, K. C., and Young, F. G. (1937) *J. Physiol.*, **91**, 352.

Rosenthal, L., Fialka, S. M., and Kanilet, J. (1939) *Amer. J. med. Sci.*, **198**, 98.

Sydenstricker, V. P., Cresslin, I. I., and Weaver, J. W. (1939) *J. Amer. med. Ass.*, **113**, 2137.

Wauchope, G. M. (1940) *Lancet*, **1**, 963.

Factors Complicating Treatment*Vitamin-A Deficiency*

J. G. Brazer and A. C. Curtis investigated vitamin-A deficiency in diabetes mellitus. Twenty young patients were studied and all showed poor dark-adaptation. Three of them complained of night-blindness and 9 of them had skin changes indicative of vitamin-A deficiency. The fundi and blood carotene level were normal in all the patients. 60,000 U.S.P. units of vitamin A daily in the form of carotene failed to improve their dark adaptability, although their blood carotene levels rose above normal. The same amount of vitamin A given as concentrated fish-liver oils rapidly rendered their dark-adaptation normal. It was therefore concluded that the lack of vitamin A in diabetics is due to their inability to convert carotene into the vitamin.

Brazer, J. G., and Curtis, A. C. (1940) *Arch. intern. Med.*, **65**, 90

DIAPHRAGM DISEASES

See also B. L. M. P., Vol. III, p. 673, and Surveys and Abstracts 1939, p. 309

Diaphragmatic Hernia*Clinical Picture*

J. J. Kristal stated that diaphragmatic hernia is not as uncommon as is usually supposed. Its apparent rarity is fostered by diagnostic difficulties but, if it is borne in mind, and radiography resorted to, it is discovered quite often. The diverse symptomatology of the condition depends on the number of organs which may be involved. Cyanotic attacks, spasmodic cough, vomiting affected by posture, and pain in the chest or abdomen are usually associated with bizarre auscultatory signs in the chest. The final diagnosis is by X-rays. Kristal reports a case in a girl of 15 months. The presenting symptom was persistent vomiting. This did not cause grave anxiety and the child did not appear seriously ill. Thirty-two hours after the onset of symptoms she was found dead in her crib, having appeared reasonably well 3 hours earlier. Necropsy revealed a strangulated diaphragmatic hernia through the left pleuroperitoneal hiatus with a left-sided pleural effusion.

Treatment

Surveys -- J. B. Hartzell discussed 68 cases of diaphragmatic hernia in children under 10 years of age, treated by operation. In this series there were 22 deaths (32 per cent), 19 of these died shortly after operation, and 3 died one to three months later. Of 12 cases showing definite signs of obstruction on admission to hospital, 8 died. A diaphragmatic hernia is a menace to the life of the patient, and early diagnosis is essential. Under 1 year of age dyspnoea, cyanosis, and vomiting are the most common symptoms, over 1 year vomiting, pain, and obstruction are more frequent. The presence of the small bowel in the thorax, and signs of a partial or complete obstruction, increase the mortality rate. Except in the case of a symptomless infant under 1 year of age, a definite diagnosis of diaphragmatic hernia should be followed by a surgical repair as soon as possible.

Hartzell, J. B. (1940) *Amer. J. Surg.*, **48**, 582.

Kristal, J. J. (1940) *Arch. Pediat.*, **57**, 76

Lipoma and Other Primary Tumours of the Diaphragm

H. C. Ballou and I. Spector record a pure lipoma arising from the diaphragm and situated behind the heart so that it was not shown in a radiograph taken during life. It was found at the necropsy of a woman, aged 45, who died with a malignant papillary adenocarcinoma of the right ovary. It measured 4 by 3 by 1.5 cm., and was the third example reported of a lipoma of the diaphragm. Reference was made to 12 previously recorded primary tumours, 4 non-malignant and 8 malignant, of the diaphragm; in several of these the clinical diagnosis had been that of a hydatid cyst.

Ballou, H. C., and Spector, I. (1939) *Canad. med. Ass. J.*, **41**, 487.

DIARRHOEA

See also B.E.M.P., Vol. IV, p. 1; and Cumulative Supplement, Key No. 305

Treatment*Apple Therapy*

I. A. Manville reviewed the use of an apple dietary in gastro-intestinal conditions such as summer diarrhoea, food poisoning, so-called intestinal influenza, etc. In such conditions all food is withheld, and a 10 per cent mixture of apple powder in water given in 6 or 8 ounce doses every 3 to 4 hours. This is continued for 1 to 4 days, depending on the severity of the disorder. With the subsidence of tympanites, tenesmus, nausea, and diarrhoea, the apple-powder water is gradually replaced by puréed baked apple, apple sauce, custard, or junket made with 5 per cent apple-powder milk. Buttermilk, and cottage and cream cheese may be added later. Other foods, largely carbohydrates and fats, are gradually added, and meats restored last.

Manville, I. A. (1940) *Arch. Pediatr.*, **57**, 302.

DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

See also B.L.M.P., Vol. IV, p. 12; Cumulative Supplement, Key No. 306, and Surveys and Abstracts 1939, p. 310

Giardia intestinalis*Clinical Picture*

P. V. Veghelyi stated that infection with the flagellate *Giardia lamblia* often produces three characteristic symptoms, namely abdominal complaints, anaemia, and retarded development. He studied the metabolism of 17 infected children, who suffered from no other disease, in order to discover how these three symptoms were produced. He found that the symptoms were all due to disorders of absorption, and he thought that this was due to the parasites covering the active area of the intestine and thus mechanically preventing absorption. He found that fat absorption and the excretion of urinary pigment were very defective in the 17 children examined. When the parasites were expelled from the intestine, the symptoms disappeared. The metabolism became normal, growth became rapid, and the anaemia recovered.

Treatment

Atebrin—I. M. Morrison and W. A. Swalm present a preliminary report on the use of atebrin (mepacrine hydrochloride) as a parasiticide against giardia. At least 50 parasiticides have been recommended in giardiasis, all characterized by failure both on laboratory and clinical grounds. This is the first report of the use of atebrin in American or English literature, but reports have appeared in foreign literature; the present authors' findings agree with these observations.

Various authors have given the incidence of giardial infestation amongst the general population as: 13 per cent of boys and 8 per cent of girls infected in 1,287 school children; 5.7 per cent infected of 2,300 soldiers serving overseas (1917), and 22 per cent of soldiers on home service infected; 13.2 per cent of 971 soldiers infected; 16.4 per cent of 4,068 soldiers convalescent from dysentery infected; 14.7 per cent of 20,237 individuals infected; 16.6 per cent among 4,270 ambulatory clinic patients infected. It is thus apparent that *Giardia intestinalis* is the most common intestinal flagellate and on these grounds the authors suggest that claims for the pathogenicity of the parasite should be regarded with the greatest caution. The possibility of giardia causing asymptomatic local inflammatory and catarrhal conditions in the small intestine is reviewed.

The present report is confined to a group of 10 carefully controlled cases but a larger group was found to react just as satisfactorily to atebrin. The dosage used was approximately the same as is employed in malaria, i.e. 1.5 grains 3 times daily taken orally for 5 days. An interval of 1 week should then elapse before a similar dose is again given; no toxic symptoms were encountered. After an average period of treatment of 1 year, 9 out of the 10 cases remained free of the parasite. The

eradication of the parasite caused complete abolition of the symptoms in some cases, moderate improvement in others, and no improvement in others. This observation may or may not indicate the pathogenicity of the parasite. In those cases in which the giardia are secondary invaders it is obvious that the symptoms will persist as long as the primary cause remains.

Morrison, L. M., and Swalm, W. A. (1939) *Amer. J. digest. Dis.*, **6**, 325

Veghelyi, P. V. (1940) *Amer. J. Dis. Child.*, **59**, 793

DIARRHOEA IN INFANCY AND CHILDHOOD

See also B.L.M.P., Vol. IV, p. 21, and Surveys and Abstracts 1939, p. 310

Summer Diarrhoea of Infants

Treatment

Pectin-agar mixtures—G. W. Kutscher and A. Blumberg experimented with pectin and agar in milk in cases of summer diarrhoea. Two preparations were made up, the first a mixture of pectin (6.3 per cent), agar (4.3 per cent), and dextrimaltose (89.4 per cent), the second, pectin (59.4 per cent) and agar (40.6 per cent). Of the 48 cases treated, 32 received the first and 16 the second mixture. It was found that with the pectin-agar-dextrimaltose mixture, normal stools were obtained in an average of 3.2 days, and with the pectin-agar mixture in 2.4 days. While the pectin-agar mixture thus appeared to be superior, in the group treated with the pectin-agar-dextrimaltose mixture, the diarrhoea had persisted for a much longer period and the infants were younger. It was necessary to ensure that the return to normal diet was very gradual.

The authors are convinced that this pectin-agar therapy, preferably with the addition of dextrimaltose, is the best form of current treatment for summer diarrhoea, a point of special advantage being the rapid elimination of toxæmia.

Kutscher, G. W., and Blumberg, A. (1939) *Amer. J. digest. Dis.*, **6**, 717

Enteritis in the Newly-Born

Treatment

Pectin-agar—P. J. Howard and C. A. Tompkins employed pectin-agar in a series of 9 out of 23 cases of enteritis in the newly-born. The method of preparing and administering the pectin-agar formulae for nurslings and older children was simply by cooking for 10 minutes 8 oz. by volume of pectin-agar powder in 24 or 16 fl. oz. of milk. New-born infants take this product readily, and it is well tolerated and retained. The usual feeding schedule is continued. Since the number of calories in this mixture is twice that usually given, the volume offered is reduced to about one-half, and the difference made up by giving water between feedings. All the infants treated with this mixture had soft stools within 48 hours, while the remainder of the group continued to have liquid stools for a week or longer.

Howard, P. J., and Tompkins, C. A. (1940) *J. Amer. med. Ass.*, **114**, 2355

DIET IN TREATMENT

See also B.L.M.P., Vol. IV, p. 38, and Surveys and Abstracts 1939, p. 311

Banana as Dietary Supplement

L. J. Roberts *et al.* supplemented the diet of 123 boys, from 8 to 16 years of age, with 2 or 3 bananas daily for a period of 9 months. The boys were inmates of an institution and a similar group of boys not receiving bananas were utilized as controls. Those on the supplemented diet increased in weight and height more than the controls. As judged by X-ray examination of the wrist bones their ossification proceeded at a slightly greater rate. It was therefore concluded that, although a minimal good diet is being given, as in the institution, it can be supplemented and the progress of the children further improved.

Roberts, L. J., Blair, R., Austin, G., and Steininger, G. (1939) *J. Pediat.*, **15**, 25

DIETITIC DEFICIENCY DISEASES

See also B E M.P., Vol. IV, p 51, and Surveys and Abstracts 1939, p 311

Deficiency of Vitamin A*Clinical Picture*

Cutaneous lesions. L. Lehman and H. G. Rapaport record 9 children of poor families, with cutaneous lesions due to vitamin-A deficiency. The lesions were symmetrical and occurred chiefly on the extremities, especially on the anterior and lateral surfaces of the thighs and legs and in the patellar region, and less often and less prominently on the lateral and posterior surfaces of the upper arm and in the olecranon region. The abdomen, buttocks, back, neck, and face were sometimes involved. The lesions were mainly horny papules formed by keratotic plugs projecting from hair follicles and often contained a broken-off hair or a coiled unerupted hair. The diameter of the papules rarely exceeded 0.2 cm. The skin was extremely dry and there might be some pruritus and loss of hair in the affected region. In these 9 cases diagnosis of the condition was confirmed by photometric observations. Improvement in visual tests was in some cases immediate with single adequately large doses of vitamin A, but others required prolonged intensive therapy. Maximal improvement in the skin condition occurred with a daily dose of from 100,000 to 300,000 international units of vitamin A in from 2 to 4 months. The authors suggest that keratosis pilaris, lichen pilaris, lichen spinulosus, ichthyosis follicularis, and other synonyms are merely descriptive terms for the cutaneous manifestations of vitamin-A deficiency.

Lehman, E., and Rapaport, H. G. (1940) *J. Amer. med. Ass.*, **114**, 386.

Nicotinic Acid Deficiency*Encephalopathic Syndrome*

N. Jolliffe *et al.* report 150 cases of an encephalopathic syndrome, a condition hitherto almost always fatal, which they believe to be caused by deficiency of nicotinic acid. It is characterized by clouding of consciousness, cog-wheel rigidities, and uncontrollable grasping and sucking reflexes, which may or may not be associated with multiple neuritis due to vitamin-B₂ deficiency, with pellagra, or with the oculomotor signs of central neuritis. Patients with this syndrome treated by hydration or hydration combined with aneurine hydrochloride almost invariably die, whereas patients treated by hydration and substances rich in the vitamin B complex show a moderate drop in mortality, and when they are treated by hydration and nicotinic acid there results a marked drop in mortality. It is probable that this syndrome represents a complete deficiency of nicotinic acid, and should be treated as such.

Jolliffe, N., Bowman, K. M., Rosenblum, L. A., and Fein, H. D. (1940) *J. Amer. med. Ass.*, **114**, 307.

DIPHTHERIA

See also B E M.P., Vol. IV, p 72, Cumulative Supplement, Key No. 324, and Surveys and Abstracts 1939, pp 41, 74, and 312.

Pathology and Morbid Anatomy*Effects of Diphtheria Toxin on Heart*

R. W. Boyle *et al.* investigated the effects of varying doses of diphtheria toxin on the hearts of 7 dogs, with regard to electrocardiographic changes, glycogen distribution, and pathological changes. The electrocardiographic changes noted consisted of various degrees of block and of abnormalities of the T wave. A mild degree of parenchymatous degeneration was invariably present, the most characteristic change being hyaline streaks throughout the muscle fibres. There was a 10 per cent rise of glycogen in the hearts of dogs given a slowly lethal injection of toxin.

A quickly lethal dose failed to produce any effects upon cardiac glycogen. In view of the cardiac increases in glycogen which occur during starvation, and of self-imposed starvation (anorexia) always present in severe diphtheritic toxæmia, the authors suggested that the moderate rise met with in such cases is the result of starvation, rather than of any specific effect of the diphtheria toxin on cardiac glycogen.

Boyle, R. W., McDonald, C. H., and DeGroat, A. F. (1939) *Amer. Heart J.*, **18**, 201.

Diagnosis

Schick Test

J. I. Warin reports the results of the Schick test in 2 groups of elementary school children, all of whom had lived in the same borough for at least 3 years, and the vast majority for much longer, so that it is reasonable to assume that they had for most of their lives been equally exposed to diphtheria infection. One group comprised those who had had diphtheria between 1930 and 1935, and the other those who had been actively immunized against diphtheria between 1930 and 1935. The two groups were comparable in regard to sex and age. The Schick-relapse rate was three times greater in the children who had had an attack of diphtheria than in the immunized group; in other words immunization gave a better Schick immunity than an attack of diphtheria.

Potassium Tellurite Test

J. F. Murray found Manzullo's potassium tellurite test to be of no value in the diagnosis of faucial diphtheria. In a series of 62 cases, he found a positive tellurite diagnosis in 38, but of these 11 (29 per cent) proved both bacteriologically and clinically not to be diphtheria. In 24 cases giving a negative tellurite test, 5 (21 per cent) proved to be definite cases of diphtheria. Positive results therefore were given by 84 per cent of diphtheria cases, but also by 37 per cent of non-diphtheria cases. The author is of opinion that there is no relationship between the test and the type of *C. diphtheriae*.

Evaluation of Various Culture Media

K. F. Cooper *et al.* discussed the comparative values of various media in the laboratory diagnosis of diphtheria. They found that Neill's blood-tellurite-agar medium gives the best result, being about 10 per cent better than Loeffler's medium. The best results are obtained if duplicate examinations are made on both media. Positive and suspect colonies should then be picked off this media and grown on heated blood-agar. The organism should be stained with alkaline methylene blue for microscopical examination. Experienced observers can tell a positive result with accuracy by looking at the colony, and it is unnecessary to stain the organisms in such cases. Virulence tests should be done on atypical strains, and injection of $\frac{1}{2}$ to 1 of an 18-hour Loeffler slope culture into the axilla of a guinea-pig with its examination after death was found to be the best method. Typical *gravis* or *intermedius* strains do not require virulence tests.

Cooper, K. F., Happold, F. C., Johnstone, K. I., McLeod, J. W., Woodcock, H. I. de C., and Zinnemann, K. S. (1940) *Lancet*, **1**, 865.

Murray, J. F. (1939) *S. Afr. med. J.*, **13**, 787.

Warin, J. I. (1940) *Brit. med. J.*, **1**, 655.

Treatment

Prevention

Immunization—V. Laura and L. Di Fulvio describe their method of preventing the spread of diphtheria from known diphtheria carriers. They sprayed or painted daily pure anatoxin on the mucosae of the nose, larynx, and pharynx, and gave weekly injections of 0.5, 1, 1.5, and 2 c.c. of anatoxin hypodermically. Seventy patients showed a complete immunity in an average of 20 days.

Laura, V., and Di Fulvio, L. (1939) *Polichinico*, **46**, 1895.

DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS, AND ASSOCIATED INJURIES

See also B.E.M.P., Vol. IV, p. 113; Cumulative Supplement, Key Nos. 326-353; Surveys and Abstracts 1939, p. 314; and p. 9 of this volume.

Delayed Healing of Fractures

Effect of Vitamin L

E. Bartolomucci investigated the claims made by various authors who attributed stimulation of bone regeneration and callus formation to the administration of vitamin E. In the author's experiments it was found that vitamin E had no effect whatsoever on the healing of fractures or on bone regeneration. Lack of vitamin E, which is usually present in sufficient quantities in normal diet, indeed produced definite slowing down in the process of bone regeneration in fractures and inhibited growth in adolescents. The author advised control of the vitamin E content of food in suspected cases in which there is slowness or even complete lack of bony regeneration or growth.

Effect of Oestrogens

G. A. Pollock publishes a preliminary report on an experimental investigation on the influence of oestrogens on calcification and on accelerating union of fractures. In a previous publication on the histological changes in the head of the femur in ununited fracture of the neck of the femur he was impressed by the great preponderance of this fracture in women more than 60 years of age; thus among 23 cases 22 were in women, further, he also noted the high incidence of senile osteoporosis of the spine in women over 50 years of age and of similar changes in the lower end of the radius. He thus was led to investigate the influence of theelin (oestrone) on callus and accelerated union of artificial fracture of the humerus in 33 rats. The animals were divided into groups treated in various ways. The results were positive and agreed with those obtained by Gardner and Pfeiffer, namely that oestrogens had a stimulating effect on the calcification of callus.

Effect of Testosterone

R. Marti discussed mal-union and non-union of bones and concludes that many fractures which unite badly respond well to the subcutaneous injection of testosterone propionate, spread over a month, given every 3 or 4 days. X-rays show a rapid growth of callus and the author recommends this method for further trial.

Bartolomucci, E. (1940) *Polichinco*, **47**, 1.

Gardner, W. U., and Pfeiffer, C. A. (1938) *Proc. Soc. exp. Biol., N.Y.*, **37**, 678.

Marti, R. (1939) *Ann. ital. Chir.*, **18**, 281.

Pollock, G. A. (1940) *Proc. Mayo Clin.*, **15**, 209.

Ununited Fractures

Treatment

N. Dunn discussed the treatment of ununited fractures. He stressed the importance of obtaining good function in the muscles surrounding the bone, by massage, etc., before operation is undertaken. Likewise the Wassermann reaction should be ascertained and if positive a full course of antisyphilitic treatment given. If the fracture is compound and has been complicated by sepsis the organism responsible should be sought and a suitable vaccine given before operation to prevent recurrence of the infection. If one of the main nerves of the limb is included in the injury it should be repaired before the bone. Dunn advocated autogenous bone graft to repair the gap between the ends and condemned the method of introducing a plate. In some cases the patient may form a false joint between the ends of the bones and be better off from the point of view of function if left like that than if operated upon. In old-standing cases of non-union of the patella and olecranon removal of the fragments of bone usually gives the best functional result. In cases of non-union of the tibia following destruction of some of the bone by osteomyelitis transposition

of the fibula gives the best results. An ununited congenital fracture of the lower third of the tibia gives very disappointing results to operative interference

Dunn, N (1939) *Brit med. J.*, **2**, 221.

Fat Embolism

Actiology

J. C. Whitaker accepts the view that the chief source of the fat in fat embolism is the injured bone. The clinical picture produced by fat emboli is that of many small transient emboli lodged in the capillaries which produce focal anaemia, oedema, or necrosis. Later leucocytes and phagocytes appear in the area to aid the process of repair. Symptoms are nearly always referable either to the lungs or the brain although the emboli may lodge in any part of the body. Symptoms appear from within a few hours to a few days and nearly all cases recover without a diagnosis having been made. Whitaker reported 2 cases, one of the cerebral type following bilateral fractures of the tibiae. The patient was comatose with a high temperature and pulse. The skin was covered with petechiae. He eventually recovered. The other case was one of fracture of both bones of the right leg. The next day the patient was dyspnoeic and had cyanosis, a leucocytosis and a raised temperature and pulse. X-ray examination showed patches of consolidation in both lungs and there were a few petechiae in the conjunctiva. A diagnosis of fat embolism was made and the patient recovered from the pulmonary signs and symptoms 4 days after the onset. Whitaker advised that, when diagnosed, the fractured limb should be taken out of the plaster cast and put into a basket splint until the symptoms have gone, in order that fat globules should not be further pressed into the veins.

J. D. Bisgard and C. Baker report experiments on rabbits designed to throw light on the causation and prevention of fat embolism as a complication in clinical practice. The factors concerned include anaesthesia, the use of the tourniquet, and drainage. The experiments show that ether anaesthesia exerts little or no beneficial influence upon embolization of fat and, if at all, only during anaesthesia or while ether is present in moderate concentration in the blood. It could not have any effect on the fat entering the blood stream 4 or 5 days after injury or operation. The use of a tourniquet during operations on bone and the gradual release, with some venous bleeding before complete release, may lessen the incidence of immediate fat embolism. The most important prophylactic measure is probably the prevention of increased pressure by drainage of the medullary canal and wound. The introduction of infection along the drainage tract is very remote, if drainage is not continued longer than 4 days. Manipulation of injured bone should be gentle and minimal. Immobilization and elevation reduce the probability of fat embolism. Fat in the sputum, and in the pulmonary capillaries, is not pathognomonic of fat embolism, because it may be derived from liquid fat in the soft tissues transported to the lungs in phagocytes.

Bisgard, J. D., and Baker, C. (1940) *Amer. J. Surg.*, **47**, 466.

Whitaker, J. C. (1939) *Arch. Surg., Chicago*, **39**, 182.

Ununited Fractures of Neck of Femur

Treatment

W. F. Gallie and F. I. Lewis describe a method of dealing with ununited fractures of the neck of the femur in the aged. After a few days of heavy traction applied with a Kirschner wire through the lower end of the femur, the fragments come into nearly as good position as would have been possible on the day of the accident. The fragments are then nailed, employing Johansson's technique with the single modification that the nail is placed close to the lower border of the neck so as to leave room for a graft above it. A half-inch hole is then bored into the neck and head parallel with the nail, and into it a suitable bone graft, cut from the crest of the ilium, the tibia, or the fibula, is inserted. This method was employed in 15 cases, in 1 case failure resulted; in 6 the fragments solidly united, and the patients were able to walk well, and in the remainder, the patients were still in bed or on crutches at the time of the report.

Gallie, W. F., and Lewis, F. I. (1940) *J. Bone Jt Surg.*, **22**, 76.

'Birth-Fractures' of Tibia*Treatment*

Bone-grafting B. McFarland described a simple method of obtaining union of 'birth fractures' of the tibia. The method consists of ignoring the zone of absorption and placing a strong bone-graft behind the tibia, implanting the graft into the back of the bone well above and below the site of non-union. This is a sort of 'bony by-pass', and carries the weight directly from the upper part of the bone to the lower.

McFarland, B. (1940) *Brit. J. Surg.*, **27**, 706

Pseudo-Fracture of Tibia

S. M. Roberts and I. C. Vogt report 12 cases of pseudo-fracture of the tibia, a rare condition occurring in children between the ages of 4 and 16 years, and affecting the upper third of the bone. There is pain at the site of the lesion and the child limps slightly. In the early stages X-rays show a little thickening only of the periosteum on the posterior surface of the bone; within a few weeks this becomes more prominent with a line of lessened density resembling an incomplete fracture. Recovery without any abnormality of the bone follows. The exact nature of the lesion is unknown, but possibly it is a chronic infection. Immobilization in plaster is the best treatment.

Roberts, S. M., and Vogt, I. C. (1939) *J. Bone Jt. Surg.*, **21**, 891

Knee-Joint*New Method of Approach*

The ideal approach to the knee-joint should give good exposure permitting thorough exploration of all parts of the joint, be adaptable to any operation which is indicated by the pathological lesion found, result in no disability, and permit of a short period of convalescence. The presence of the patella is the chief obstacle to this ideal, as is indicated by a study of the standard methods of approach to the knee-joint, which appear to have been influenced by the conception that the patella is a necessary structure indispensable to the proper functioning of the joint. That the patella can be removed without resulting in any loss of function was recently shown by R. Brooke, who removed it in 30 cases of fracture, with excellent functional results and claimed that its presence is incidental and is a deterrent rather than an aid to the movement of the joint. This work led V. O. Mader to evolve a new approach to the knee-joint with the advantage that, when excision of the joint is contemplated, an exploration of the joint may first be made, and the final decision as to whether a resection is to be carried out need not be made until the lesion is exposed and examined. His technique is as follows. After administration of a spinal anaesthetic, the patient is placed in the supine position, with the knees flexed over the end of the table. A curved infra-patellar incision is then made, the skin-flap dissected upwards, and the patella and quadriceps tendon exposed. The tendon overlying the patella is split longitudinally and the incision carried upwards into the quadriceps tendon and downwards into the patellar tendon. The patella is dissected out through this incision with the help of a sharp periosteal elevator. The joint is then exposed and the incision may be carried up or down as far as desired. Retraction gives an excellent view of the joint. If a mistake in diagnosis has occurred, the joint may be closed without damage.

Brooke, R. (1937) *Brit. J. Surg.*, **24**, 747

Mader, V. O. (1940) *Canad. med. Ass. J.*, **42**, 17

Lower Limb*Volkmann's Ischaemic Contracture*

V. Riche *et al.* found very few records of Volkmann's ischaemic contracture of the lower limb; they described a case of fracture of both thighs and of the right ischio-pubic and ilio-pubic bones in a man, aged 42, without any history of pathological conditions or arteriosclerosis. There was retardation of consolidation of the fracture and a progressive retraction of the ham-strings. The authors describe

attempts at treatment of Volkmann's ischaemic contracture. Injections of novocain (procaine hydrochloride) into the lumbar sympathetic were of no avail. Massage, electrotherapy, and radiotherapy gave a certain relief. Most authors have adopted surgical methods: aponeurotomy to regain circulatory integrity of the limb and sympathetic operations have been tried with success by Jones and by Dieulafé respectively but these 'pathogenic' operations are very difficult. Palliative measures include tenotomy, osteotomy, and operations on the joints according to the site of the contracture.

Dieulafé, R. (1935) *Rev. Orthopéd.* **22**, 18.

Jones, G. (1935) *J. Bone Jt Surg.*, **17**, 659.

Riche, V. Aussilloux, J., and Ginestie, J. (1939) *Pr. méd.*, **47**, 1173.

Fracture of Ulna

Associated with Dislocation of Head of Radius

F. Klages reported 12 patients seen during 11 years and suffering from fracture of the ulna with dislocation of the head of the radius. In 3 cases of fresh injury, conservative treatment, consisting in reduction both of the fracture and of the dislocation, was successful and resulted in complete, or nearly complete, function. In 2 cases of fresh injury, closed reduction was unsuccessful and surgical treatment was carried out. In the first case reposition was easily effected, but in the second the radial head had to be resected. There was complete restoration of function following this form of treatment. In 6 cases of old injury, seen 2 to 11 months afterwards, operative reduction was satisfactory in 2.

Klages, F. (1939) *Msehr. Unfallheilk.*, **64**, 368.

Minor Fractures

Treatment

Local anaesthesia—H. Cullumbine defined a minor fracture as one in which there is no displacement and no possibility of displacement. He treated 100 such cases with local anaesthesia. A 2 per cent solution of procaine hydrochloride was injected into the haematoma between and around the ends of the fractured bone. The patient was used only in second degree fractures of the ankle and those in which there was much oedema. Fractures in many sites, such as the ankle, phalanges, fibula, and great trochanter of the femur, were treated successfully by this method. Pain quickly disappeared and function was restored very rapidly. Cullumbine also reported many cases of sprain treated successfully by the same method.

Cullumbine, H. (1939) *Lancet*, **2**, 552.

Fractures of Spine

Clay-Shoveller's Fracture

R. D. McKellar Hall reports 13 cases of clay-shoveller's fracture, a term applied to a fracture of one or more spinous processes of the lower cervical or upper thoracic vertebrae, and occurring in most cases in relief workers engaged in shovelling clay. The usual history is that the labourer throws up a shovelful of clay, the clay sticks to the shovel, the worker feels a sudden stab of pain and sometimes hears a crack somewhere between the shoulders, and is unable to continue at work. It is suggested that the cause of clay-shoveller's fracture is closely associated with the origins and actions of the trapezius (middle portion), the rhomboideus major and minor; the serratus posterior superior acts merely as an accessory to these muscles, for, when the worker is in the act of throwing, this muscle is probably in full contraction, thus helping to fix the chest. The fracture may be explained by three possible mechanisms: direct muscle violence; reflex muscle contraction; and whip-like pull transmitted through the supraspinal ligaments. The patient complains of the pain between the shoulders, rendered worse on forward stretching of the arms, or on attempting to lift anything. Examination reveals tenderness of the spinous process at the site of fracture, and tenderness along the course of the rhomboid, on one side. Treatment consists in early removal of the detached fragments.

Hall, R. D. McK. (1940) *J. Bone Jt Surg.*, **22**, 63.

Dislocation of Elbow Joint

Treatment

According to M. G. Kini the treatment of elbow dislocation, when the patient is seen immediately after the accident, is simple, provided the following principles are observed: X-ray examination before reduction and preliminary investigation for nerve injuries; reduction of the dislocation under anaesthesia and a second X-ray examination after reduction; proper splinting of the dislocation after reduction to prevent effusion into the joint and the surrounding tissues; enforcement of sufficient rest to permit the completion of the process of healing inside the joint, and, to restore function, institution of the graduated active exercises with physiotherapy after removal of the splints. The most important complication arising from a dislocation of the elbow is the formation of new bone (myositis ossificans) which can be prevented. When a dislocation remains unreduced, or when the elbow is fixed, due to the formation of new bone, excision of the elbow is advisable.

Kini, M. G. (1940) *J. Bone Jt Surg.* **22**, 107.

Bone Grafting

J. B. Chester describes a new simplified technique for bone grafting consisting of mechanically separating the bone fragments for freshening and shaping, holding them tightly approximated while the bone graft is cut and fixed, and finally fixing the fragments immovably in the cast until union is completed. He suggests a method for fixing the free upper end of a sliding bone graft in its bed by the transfixion of the graft and cortex of the tibia with a Kirschner wire which may later be removed without disturbance of the wound, or the fragment, or open operation.

Chester, J. B. (1940) *Surg. Gynec. Obstet.* **70**, 819.

DISSEMINATED SCLEROSIS

See also B.F.M.P., Vol. IV, p. 187, Cumulative Supplement, Key No. 354; and Surveys and Abstracts 1939, p. 316.

Aetiology

It has been suggested that disseminated sclerosis may be due to a blood enzyme which breaks down the myelin sheaths of the nervous system. C. H. Richards and H. G. Wolff investigated this question in normal persons, in patients with disseminated sclerosis, and in sufferers from other diseases. There was not any difference in the enzyme activity of patients with disseminated sclerosis and other persons. Debilitating conditions lowered the enzyme activity and quinine hydrochloride in vitro inactivated the lipase and choline esterase in the serum of all the subjects. It increased the activity of the esterase. The level of the serum enzymes varied greatly in individuals, but remained constant for the individual over long periods. In view of the difficulty of assessing such a complicated process as serum enzyme activity Richards and Wolff do not consider that these experiments disprove the hypothesis in disseminated sclerosis, but they cast doubt upon it.

After examination of 96 twins, one of whom was a definite case of disseminated sclerosis, K. Thums could not demonstrate that heredity was of any importance in the aetiology of this disease. Heredity seemed not even to give rise to a disposition to the disease. In consequence of an examination carried out in relatives of patients affected with disseminated sclerosis, Curtius had supposed in patients affected with this disease a certain poor inborn quality of the central nervous system. This investigation, as well as a statistical examination suggested by Luxenburger, have led Thums to admit that inborn factors may perhaps be of slight value in the aetiology of disseminated sclerosis. Essentially, however, the disease is caused by environmental factors.

Allergy

R. L. Baer and M. B. Sulzberger investigated the part played by allergy in 40 cases of disseminated sclerosis, from the point of view of atopic hypersensitivity. Asthma, hay-fever, and atopic dermatitis are examples of this type of allergy. The family history of the patients was investigated and intradermal tests were made

with the protein fractions of foods and other materials. In 30 of the patients 10 had a positive family history or skin test or both. This incidence (33 per cent) is not significantly greater than that of the normal population. It is, of course, possible that some other form of allergy may play a part in the aetiology of disseminated sclerosis and that the symptoms of multiple sclerosis may sometimes be produced by atopic allergy. The Prausnitz-Kustner reaction of the cerebrospinal fluid was investigated in one atopic patient with inconclusive results.

Baer, R. I., and Sulzberger, M. B. (1939) *Arch. Neurol. Psychiat., Chicago*, **42**, 837.

Richards, C. H., and Wolff, H. G. (1940) *Arch. Neurol. Psychiat., Chicago*, **43**, 59.

Thums, K. (1939) *Munch. med. Wschr.*, **86**, 1634.

Clinical Picture

Trigeminal Neuralgia

B. Finesilver agrees that, though paraesthesiae and objective sensory upsets are common, pain is rare in disseminated sclerosis. Trigeminal neuralgia, however, is occasionally present and differs in no way from orthodox tic douloureux. He reports 3 cases in which the predominant and initial symptom was facial pain. Relief was given by peripheral measures, such as alcoholic injection and resection of the sensory roots. It was therefore assumed that the sclerotic plaque was peripherally situated and responsible for the pain. None of the cases came to necropsy. Other workers have failed to demonstrate peripheral lesions but have shown plaques in the region of the sensory root of the 5th cranial nerve in these cases. Presumably therefore trigeminal neuralgia in disseminated sclerosis may be peripherally or centrally caused. Treatment differs in no way from that used for other varieties of trigeminal neuralgia.

Finesilver, B. (1939) *J. Nerv. ment. Dis.*, **90**, 757.

Treatment

Leucithin

In cases of disseminated sclerosis, lumbar injection of an emulsion of 0.1 to 0.2 cc. leucithin in 5 c.cm. of physiological saline was given by Minea. The leucithin was purified by repeated washing in alcohol, and was preserved in sterile airtight ampoules. For injection isotonic saline was added, this emulsion was warmed up to body temperature and was injected after removal of a few c.cm. of cerebrospinal fluid. Only slight disturbance resulted. After an injection the patient had to lie in a horizontal position for 48 to 72 hours. Usually 3 or 4 injections were made at an interval of 8 to 10 days. After some weeks a new series of injections may be given. One hundred and thirty patients were treated in this way, in 88 per cent complete remission resulted or a remission sufficient for the patient to return to his work. The good effect was supposed to result from true biochemical antilipase reaction, liberating the affected tissue from pathological lipase.

Nicotinic Acid and Vitamin B₁

M. T. Moore discussed the treatment of disseminated sclerosis with nicotinic acid and vitamin B₁. Many factors have been considered in the aetiology of this condition, but recently some vascular lesion has been cited as the possible cause. Nicotinic acid has been found to produce marked flushing of the skin and Moore showed that it caused hyperaemia in the brain and spinal cord of the cat. This led him to treat 5 cases of disseminated sclerosis with the drug. It was given intramuscularly and intravenously on alternate weekdays, 60 to 120 mg. and 60 to 160 mg. being given respectively. 10,000 international units of vitamin B₁ were also given intravenously at the height of the cutaneous hyperaemia. After a time the two drugs were given in a combined solution, 10 c.cm. intramuscularly into the buttock. It was found necessary to give this solution warmed and in a warm syringe if the full effect of the hyperaemia were to be produced. All the cases responded favourably although they were chronic and had not been markedly affected by other treatments. During the hyperaemia of the skin the cerebrospinal fluid pressure

rose, furnishing additional evidence that the hyperaemia also extended to the brain and spinal cord

Moore, M. T. (1940) *Arch. intern. Med.* **65**, 1

Von Minca, I. (1939) *Munch. med. Wschr.*, **86**, 1038

DIVERTICULOSIS AND DIVERTICULITIS

See also B.E.M.P., Vol. IV, p. 207; Cumulative Supplement, Key No. 355, and Surveys and Abstracts 1939, p. 316

Meckel's Diverticulum

Clinical Picture

T. Persson, reviewing 15 cases of Meckel's diverticulum, concluded that the condition might be suspected in the following circumstances: delayed healing of the umbilicus after birth; adenoma of the umbilicus and other congenital conditions in the abdominal wall; umbilical colic with local tenderness; and profuse bright-red haemorrhage from the intestines, especially in children. Perforation of a Meckel's diverticulum results from mechanical perforation of a foreign body, and not as a result of diverticulitis. There are few clinical manifestations from perforation, and the symptoms of peritonitis may be mild.

Heterotopic gastric mucosa causing massive rectal haemorrhage—G. A. Fleet records a case of ulceration of areas of misplaced gastric mucosa in a Meckel's diverticulum and in the ileum, the latter being perforated about 3 feet from the ileo-caecal valve. The patient, a boy aged 6½ years, had had 3 previous attacks of abdominal pain, vomiting, and the passage of a little blood in the stools, in the fourth attack the amount of blood passed by the rectum was very considerable. A diagnosis of haemorrhage from an ulcerated area of ectopic gastric mucosa was confirmed at laparotomy, at which the diverticulum and the affected part of the ileum were removed. In a review of the subject it is pointed out that, not only may gastric mucosa be displaced into the small intestine, but that in other cases intestinal mucosa may be present in the mucosa of the stomach. It has been suggested that this heterotopia may be (a) congenital, a form of dysembryoma, or (b) acquired and due to altered environment, inflammation, or some unknown stimulus. Recent reports show that ulceration of Meckel's diverticulum is not uncommon, that 85 per cent of the cases are in males, 33 per cent under the age of 10 years, and that 30 per cent prove fatal. The absence of mucus mixed with the blood helps in the diagnosis from intussusception. The causes of the passage of blood from the rectum differ in adults and in children, the common causes in adults, such as piles, rectal cancer, chronic peptic ulcer and hepatic cirrhosis, are rare in children, in whom intussusception, rectal polyp, rectal prolapse, forms of purpura, and acute infections should be borne in mind.

Fleet, G. A. (1940) *Canad. med. Ass. J.*, **42**, 216

Persson, T. (1939) *Acta chir. scand.*, **82**, 530

DRUG ADDICTION

See also B.E.M.P., Vol. IV, p. 246; Cumulative Supplement, Key No. 359, and Surveys and Abstracts 1939, p. 318

Some Forms of Drug Addiction

W. P. Kennedy describes some forms of drug addiction and first points out that the original meaning of the word 'addiction' in Roman law was the formal handing over to a court, and from this came the conception of being bowed to a master, and so the modern meaning of using a drug in excess of the medical indication and in response to a craving, which the drug induces or increases. Indian hemp, marihuana in America, hashish (usually smoked), bhang (drunk), and charas (usually eaten) in the Orient, cause horrible crimes of violence, often without any motive. The addict is often led into indulgence in the 'white' drugs, morphine, heroin, and cocaine. Initiates are much more readily won over to the seductions of 'Mary Jane'

or the 'reefer' cigarette, than is the case in most drugs. The usual effects are hallucinations of space and time, and often of colour, such as kaleidoscopic visions of brilliant hues. Changing designs of wheels and spirals are common, and it has been suggested that the first chapter of Ezekiel is a vision seen under the influence of hashish. In South Africa dakha (hashish) smoking is rendered more difficult to suppress by the ease with which the weed can be grown. In 1931 this addiction aroused the attention of the Canadian authorities, and 3 years ago it was reported that its smoking occurred in London, but not widely spread. The hallucinations produced by mescal or peyote are even more brilliant and prolonged than those due to hashish, it also produces a strange sensation of being dematerialized. Codeine ethylmorphine, and some of the barbituric series have recently been found to give rise to cases of true addiction. Eating tea leaves has produced violent intoxication without euphoria in women, and in Tripoli and Egypt the black tea habit, the leaves being repeatedly boiled, has been used as a substitute for drugs difficult or too costly to get, it has probably been adopted to obtain a narcotic or aphrodisiac effect. Evidence that there is an aspirin habit in Great Britain is brought forward

Kennedy, W. P. (1940) *Pharm. J.*, 4 ser., **90**, 169.

Alcoholism and Drug Addiction in War-Time

W. N. East reviews these conditions from the experience of the 1914-18 war and shows how much better placed the country is now as a result. In the years 1910-1914 the number of persons dealt with summarily in England and Wales for drunkenness and so forth averaged 193,354, and in 1914 and 1916 alcoholism was seriously diminishing efficiency. As early as August, 1914, the Intoxicating Liquor (Temporary Restriction) Act was applied to civilians and supplemented the restrictive orders of the naval and military authorities in naval and military areas. A number of other prohibitions were introduced by the Defence of the Realm Act. The manufacture of cocaine without a licence was prohibited, and the possession of cocaine was made a summary offence unless the drug had been supplied in accordance with a prescription, or the holder of the drug was licensed to manufacture it. An order of the Army Council prohibited the sale or supply of coca, codeine, diamorphine, Indian hemp, opium, morphine, sulphonal and its homologues, barbitone, benzamine lactate, benzamine hydrochloride, and chloral hydrate to any member of His Majesty's Forces, not being a registered medical practitioner, registered dentist, or registered veterinary surgeon except under certain stated conditions. The war-time restrictions reduced the convictions for drunkenness to 31,119 in 1918, but they rose to 61,376 in 1919. From 1920 to 1932 there was a continuous fall in the number of convictions for offences of this kind, but from that year there was a continuous rise, and in 1937, the last year in which the figures were available, the numbers amounted to 52,425. Since 1930, however, half the naval ratings entitled to receive the rum ration have preferred to receive the alternative daily allowance of three-pence. The country entered the present war in a position strengthened by the legislation of the recent past, such as the increased duty on beer, wine, and spirits, and, as mentioned above, by the experience of 1914-1918.

East, W. N. (1939) *Brit. J. Inebriet.* **37**, 132.

DRUG ERUPTIONS

See also B.I.M.P., Vol. IV, p. 261, Cumulative Supplement, Key No. 360; and Surveys and Abstracts 1939, pp. 176 and 319.

Due to Insecticide

R. D. G. P. Simons and J. Simons-Jantzen described cases of insecticide dermatitis caused by the commercial insecticide 'flit'. Many people erroneously use this substance to counteract insect bites. It contains oil of lemon and oil of turpentine which cause irritation in the skin. Warmth and clothing aggravate the painful itching dermatitis caused, and the authors point out that it would be safer to extract the noxious agent before commercial distribution of the insecticide.

Simons, R. D. G. P., and Simons-Jantzen, J. (1939) *Geneesk. Tijdschr. Ned.-Ind.*, **79**, 2442.

DWARFISM AND INFANTILISM

See also B.E.M.P., Vol. IV, p. 277, and Surveys and Abstracts 1939, p. 319.

Aetiology

Relation between the Growth-promoting Effects of the Pituitary and the Thyroid Hormone

H. M. Evans *et al.*, experimenting with parathyroidectomized and hypophysectomized-thyroidectomized rats and substitutional treatment, arrived at the following conclusions on the relation between the growth-promoting effects of the pituitary and thyroxine. Gigantism brought about by the administration of extracts of the anterior pituitary does not depend on the presence of the thyroid, but is greater when it is present. Growth promotion of thyroidectomized or thyroidectomized-hypophysectomized animals in excess of the normal (gigantism), brought about by anterior pituitary extracts, is only maximal when thyroxine is given at the same time. Thyroxine, which promotes the growth of thyroidectomized animals, does not have this effect when given to thyroidectomized-hypophysectomized animals. Characteristic ovarian changes occur in animals with thyroidectomy of long standing, and consist essentially in the substitution of medullary for cortical activity and a growth of the so-called medullary or hilum tubules. In extreme cases these structures form the chief part of the ovary, the ovarian follicles, corpora lutea, and normal interstitial tissue having disappeared. The administration of thyroxine to these thyroidectomized females prevents the development of the hilum tubules, but extracts of the anterior pituitary do not have this effect.

Evans, H. M., Simpson, M. E., and Pencharz, R. I. (1939) *Endocrinology*, **25**, 175.

DYING, CARE OF THE

See also B.E.M.P., Vol. IV, p. 313

Voluntary Euthanasia

J. Purves-Stewart in advocating the legalization of voluntary euthanasia pointed out what euthanasia is not—it is not proposed that medical practitioners should be allowed to kill off patients with incurable diseases; that anyone who wishes to commit suicide should be allowed, much less encouraged to do so—that anyone who is morbidly depressed, tired, or bored with life, or who feels himself or herself a burden to their relatives should be given a lethal drug; or that congenital imbeciles, patients with chronic dementia, or those with certain hereditary physical or mental disabilities should be painlessly deprived of life. There are ethical, legal, and medical obstacles to voluntary euthanasia. The Roman Catholic Church forbids it. As the English law stands, euthanasia may be technically classified as murder, homicide, or suicide, but the State recognizes several forms of justifiable homicide, as in self-defence, and in times of war not only approves of homicide, but organizes and encourages it. Medical diagnosis is not infallible, and to meet this objection it is proposed as a scrupulous safeguard that no individual doctor shall in future have the responsibility of deciding, or refusing, to comply with the patient's wish; but that the doctor should call into consultation a medical colleague to decide on medical grounds whether the patient is fatally ill, and whether he or she should be condemned to continue to suffer. The patient alone should be considered and not the wishes of his or her relatives.

Purves-Stewart, J. (1939) Pamphlet published by the Voluntary Euthanasia Legislation Committee.

DYSMENORRHOEA

See also B.F.M.P., Vol. IV, p. 353, and Surveys and Abstracts 1939, p. 321.

Treatment

Oestradiol Benzoate

S. H. Sturgis and F. Albright treated 25 cases of so-called essential severe dysmenorrhoea with oestrin. By this treatment anovulatory bleeding was established and it was painless. Therefore it appears that ovulation is necessary for dysmenorrhoea to occur. One c.c. of an oily solution of oestradiol benzoate was injected intramuscularly every third day. A series of injections consisted of from 3 to 14. The result depended upon how soon in the month the injections were started. If the series was given within the first week after the onset of the menses, the next period was invariably painless. But this course had no effect upon the dysmenorrhoea of the next period unless the injections were repeated at the same time during the cycle. Biopsy showed that this treatment prevented the formation of a secretory endometrium and therefore of ovulation. These observations can be used in other clinical problems. Thus in cases of sterility, if dysmenorrhoea occurs, ovulation must be taking place. A few of the patients received the treatment on alternate months for at least a year and they experienced a gradual improvement in the severity of the cramps in the months when no injections were given.

Testosterone Propionate

U. J. Salmon *et al* treated 30 patients suffering from dysmenorrhoea with testosterone propionate. The dose recommended was 250 to 350 mg. given during one menstrual cycle. Twenty-six of the 30 women were relieved of their symptoms. Larger doses, up to 500 mg., produced virilism. There was deepening of the voice, enlargement of the clitoris, facial hirsuties, and suppression of menstruation. There were also signs of oestrogen deficiency, namely atrophic vaginitis, hypoplasia of the endometrium and 'negative' vaginal smears. These effects were thought to be due to inhibition of the gonadotrophic function of the pituitary producing a suppression of ovulation and oestrogen and progesterone formation. It was suggested that the value of the hormone in the treatment of dysmenorrhoea might be due to this suppression because functional dysmenorrhoea might be caused by an androgen deficiency.

Injection of Testosterone Propionate

A. R. Abarbanel reported 10 cases of dysmenorrhoea which were treated by percutaneous administration of testosterone propionate. The drug acts by inhibiting contractions of the uterus which are the immediate cause of dysmenorrhoea. It was applied, the axillary region usually being chosen, in either an oily or ointment base. The oily base is more efficient but is less liked by the patients. The dose required is 3 to 6 times greater than the subcutaneous dose and in this series ranged from 20 to 90 mg. per menstrual cycle. Absorption is greater if the skin to which the drug is applied is first shaved. The patients should first receive testosterone by injection to see if they respond to it and what dose will be necessary for percutaneous administration. This method is more successful than intramuscular injection but not so good as subcutaneous injection. The treatment failed in only 1 case in this series and there were no unpleasant side-effects such as masculinization.

Abarbanel, A. R. (1940) *Endocrinology*, **26**, 765

Salmon, U. J., Geist, S. H., and Walter, R. I. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 264

Sturgis, S. H., and Albright, F. (1940) *Endocrinology*, **26**, 68.

DYSPHAGIA

See also B.F.M.P., Vol. IV, p. 377.

Causes

Hypovitaminosis-B

I. R. Jankelson reported 6 cases of dysphagia, ascribed to vitamin-B deficiency,

and relieved by adequate vitamin-B administration. The patients were females, with ages ranging from 22 to 65, and the dysphagia had lasted from 2 weeks to 17 years. The diagnosis of dysphagia due to vitamin-B deficiency was made by elimination of all other causes, by careful analysis of the patients' diet, and by observing the results of vitamin-B administration. Treatment consisted of liver extract and aneurine hydrochloride intramuscularly, or vitamin-B complex by mouth, in some cases supplemented by nicotinic acid orally

Jankelson, I. R. (1940) *Amer. J. digest Dis.*, **7**, 252

EAR DISEASES

See also B.E.M.P., Vol. IV, p. 402, Cumulative Supplement, Key Nos. 374-384, Surveys and Abstracts 1939, pp. 86, 94, and 322, and p. 46 of this volume

Diagnosis

Differential Stain for Hair Cells of Organ of Corti

I. P. J. MacNaughton and F. W. Peet described a differential stain for hair cells. Whilst staining the organ of Corti they noted that the hair cells gave a specific reaction to Mallory's stain. Because the aniline blue in the stain obscured the finer details of the cell they evolved another method whereby the stain was used for a longer period in greater dilution. The slides were stained individually and should be frequently inspected during the staining to ensure a successful result. Celloidin sections were used and stained in the following manner:

Section in distilled water	-	10 minutes
0.1 per cent acid fuchsin	-	1 hour to 24 hours

Inspect from time to time to see if the hair cells are stained

1 per cent phosphomolybdic acid	-	5 minutes
Wash in distilled water	-	5 minutes

Mallory's connective tissue stain (modified)

Aniline blue (water soluble)	-	0.5 g
Orange G	-	2.0 g
Oxalic acid	-	2.0 g
Distilled water	-	100 c.c.m.

Of this add 1 c.c.m. to 50 c.c.m. of distilled water and stain for 1 to 2 hours

Rinse in distilled water
Differentiate in 95 per cent alcohol.
Clear by xylol blot method
Mount in canada balsam

The hair cells appeared scarlet against the supporting cells and tectorial membrane which stain blue.

MacNaughton, I. P. J., and Peet, F. W. (1940) *J. Laryng.*, **55**, 113

Diplacusis

Localizing Symptoms of Disease of Organ of Corti

G. F. Shambaugh records diplacusis, one sound heard as two, as diagnostic of disease of the organ of Corti. Usually the same sound is heard at a different pitch by the 2 ears. The test for diplacusis is made with a tuning-fork and may be positive, although the patient is unconscious of the disorder. Out of the author's 45 patients, 33 showed primary nerve deafness. Five cases of suppurative otitis media also had acute serous labyrinthitis. Diplacusis was also present in cases of haemorrhage into the labyrinth, trauma to the membranous labyrinth, and in labyrinthitis resulting from focal infection or allergy. It also occurs in nearly all cases of Ménière's syndrome with defective hearing, and it is therefore concluded that this syndrome is due to either allergic or focal disease of the membranous labyrinth. In Ménière's syndrome the deafness is for low and high tones and in the early stages normal hearing may return.

Shambaugh, G. F., Jnr. (1940) *Arch. Otolaryng., Chicago.*, **31**, 160.

Otomycosis*Treatment*

Metacresyl acetate and thymol—M. O. Dart stated that otomycosis occurs much more frequently than is generally supposed, and is often overlooked in the treatment of otitis externa. Powdered silver picrate, which has been advocated, was found to be ineffective in treatment. The author found that the most effective fungicidal drugs now available are metacresyl acetate and thymol. The canal is first cleared of debris by irrigation, then dried by warm air. It is then packed with absorbent cotton-wool saturated with metacresyl acetate. This packing is removed by the patient next morning. Six drops of a 1 per cent solution of thymol in 70 per cent alcohol is placed in the ear and allowed to remain in for 5 minutes. This treatment with thymol drops is repeated twice a day for 5 days, then a thymol iodide powder is insufflated twice a day for 5 days.

Dart, M. O. (1940) *Arch. Otolaryng., Chicago*, **31**, 885.

Acute Otitis Media*Treatment*

Sulphonamide compounds—V. G. Horan and S. G. French employed sulphanilamide in 621 cases of suppurative otitis media. In this series mastoiditis occurred in only 3.4 per cent, as compared with an incidence of 22.7 per cent in a previous series of 607 cases treated before the introduction of this drug. Treatment in all cases consisted of a course of an emulsion of sulphanilamide (colsulanyde), begun as early as possible, and continued until a total of 40 g. of the drug had been given. In some of the more acute cases protosil rubrum was given by injection. In cases in which pneumococci were isolated, sulphapyridine was employed, instead of sulphanilamide.

Recurrence after inadequate sulphonamide therapy. According to J. M. Converse sulphanilamide treatment in haemolytic streptococcal infections does not lead to the formation of antibodies, and too early cessation of the treatment allows the infecting organisms to become fully virulent again. Laboratory bacteriological investigation, rather than clinical symptoms and signs, should indicate when to withdraw the drug. He reports 4 cases of acute streptococcal otitis media which had received 16 g. of sulphanilamide in 3 days; the otitis media recurred after the cessation of the treatment. In 3 other cases late meningitis followed withdrawal of the drug. All the patients recovered, but further large doses of sulphanilamide were required to sterilize the cerebrospinal fluid.

Converse, J. M. (1939) *J. Amer. med. Ass.*, **113**, 1383.

Horan, V. G., and French, S. G. (1940) *Lancet*, **1**, 680.

Chronic Suppuration of the Middle Ear*Treatment*

Argyrol displacement. W. Ogilvy Reid described the treatment of chronic otorrhoea and otorrhoea not requiring operation by argyrol displacement. Cases with a frankly purulent or thick muco-purulent discharge do best, whereas those with a purely mucoid discharge respond better to ionization. The ear is thoroughly cleaned then filled with 10 per cent argyrol (mild silver protein) solution to the lower level of the tragus. A Siegle speculum is then fitted into the meatus with the bulb compressed. The bulb is allowed to expand gradually when it is certain that the connexion between the speculum and the meatus is airtight. If it is not airtight the gap may be occluded with cotton wool. The procedure is repeated 3 times, and the treatment is carried out daily. About 12 treatments are necessary to effect a cure. In a series of 166 cases, 62.07 per cent were cured. Most of the others required surgical treatment. It is essential to eradicate nasopharyngeal infection in all these cases.

Reid, W. O. (1939) *Brit. med. J.*, **2**, 1271.

Operations on the Ear

Mastoidectomy

Effect on hearing.—J. H. Maxwell and H. J. Richter analyse 50 cases of radical mastoidectomy in order to gain further knowledge about the effect of the operation on hearing. In this series patients over the age of 45 showed the greatest post-operative loss of hearing. Residual hearing was considerably diminished in patients in whom otorrhoea had existed for less than 4 years before operation. Pre-operative labyrinthine irritability appeared to be without any relation to post-operative hearing. The results suggested that rapid healing of the wound carries a better prognosis with regard to residual hearing. The greatest loss of hearing occurred in patients in whom pre-operative hearing was best, and the greatest gain in hearing was in those in whom pre-operative loss of hearing was more than 40 decibels in the conversational range. Of the 50 cases, complete healing with freedom from discharge was obtained in 84 per cent; in the other cases some mucoid discharge, coming from the Eustachian tube, persisted. In 44 per cent of the cases post-operative gain in hearing, averaging 5.6 decibels, resulted, in 8 per cent no improvement occurred; and in 48 per cent a loss of hearing, averaging 9.4 decibels, ensued.

E. H. Tomb analysed 100 consecutive simple mastoidectomies. He found that closure of the periosteum assisted formation of new bone. Mastoiditis was more frequent in patients between the ages of 5 and 10, and the incidence of mastoiditis was highest in February and March, and lowest in August, September, and October. The best time for operation was about the third week of otitis media, before then there was little localization, and later than that the vital visceral structures were more often affected. Simple mastoidectomy was sufficient in acute mastoiditis superimposed on chronic purulent otitis media. The formation of new bone was not found in recurrent mastoiditis in less than one year after the previous operation. A revision mastoidectomy was indicated in the presence of sepsis with threatening symptoms, or when healing had failed. In 54 per cent of the cases cultures of material from the mastoid yielded a *Streptococcus haemolyticus*, and in 12 per cent a pneumococcus. Streptococci were associated with fulminating symptoms and numerous complicating lesions, whereas pneumococci caused practically no symptoms, but extensive destruction of bone.

Maxwell, J. H., and Richter, H. J. (1940) *Arch. Otolaryng., Chicago*, **31**, 426.
Tomb, E. H. (1940) *Arch. Otolaryng., Chicago*, **31**, 478.

ECZEMA

See also B.E.M.P., Vol. IV, p. 447; Cumulative Supplement, Key No. 386, and Surveys and Abstracts 1939, pp. 63 and 326.

Clinical Picture

Infantile Eczema

Sudden death.—J. H. T. Davies reported 3 consecutive cases of infantile eczema which had a fatal outcome. The accident is peculiar to infants with true infantile eczema; it occurs during the first year of life; large fat over-nourished infants are more susceptible than undernourished infants; most of the cases occur during spring; most, if not all, cases occur in hospital, or away from the mother; the accident generally occurs within the first few days of hospitalization; its occurrence is sometimes preceded by improvement in the eczema; and necropsy never appears to disclose a sufficient cause of death. The cause of the complication is still obscure. No detail of local treatment, or of general nursing, nutrition, or management has the slightest influence on the incidence or course of the complications.

Davies, J. H. T. (1940) *Brit. J. Derm.*, **52**, 182.

Treatment

Vitamin-B Complex

K. P. Kristensen and S. N. Vendel stated that the treatment of eczema is difficult because its essential cause is unknown. Many factors sometimes regarded as the

cause of the condition are probably exciting causes only. Skin diseases often occur in vitamin deficiencies, for example, the symmetrical dermatitis of pellagra. The vitamin-B complex also includes many skin factors. These facts led Kristensen to treat those suffering from eczema by saturating the system with vitamin-B complex. In more than 100 cases of typical eczema the treatment produced striking results, whether given by mouth or by injection. It had no such specific results in any other skin disease. It was therefore suggested that eczema may be due to a deficiency of the vitamin-B complex. In 13 chronic and 7 acute or subacute cases the results of treatment were excellent. The patients were treated with bevital Leo, a Danish preparation, given as tablets, each one equivalent to 15 g. of yeast, or as a paste, each 1 c cm. equivalent to 20 g. of yeast. About 12 tablets a day were usually given. When the patient was cured, it was found that smaller maintenance doses would keep him free from eczema. It was thought that the vitamin-B₂ complex contained in vitamin-B is responsible for the cure of the eczema.

Kristensen, K. P., and Vendel, S. N. (1940) *Lancet*, **1**, 170

EMPHYEMA

See also B I M P., Vol. IV, p. 520

Acute Empyema

Actiology

Br. abortus infection.—R. H. Macdonald reports a case of left peritonissillar abscess followed by a left empyema. Paracentesis showed a seropurulent effusion fluid which, after repeated tapplings, became purulent. A smear contained Gram-negative diplococci but no growth was obtained. As the patient had given a positive agglutination test for *Br. abortus* 3 months previously, the fluid was cultured and gave a pure growth of this organism. Rib resection with external drainage was then established and the patient completely recovered. The case was reported because, in the absence of pyogenic organisms in the smear or culture of an empyema, it is usually assumed to be tuberculous in origin.

Macdonald, R. H. (1939) *J. thorac. Surg.*, **9**, 92

Tuberculous Empyema

Treatment

Sulphapyridine.—G. S. Erwin reports on the use of sulphapyridine in 3 cases of secondarily infected tuberculous empyema, a condition characterized by prolonged high fever, progressive emaciation and deterioration, spreading pulmonary disease, amyloid change, and finally death from toxæmia. Even after adequate drainage these patients are seldom fit for the thoracoplasty which seems to offer the only prospect of recovery, and conservative treatment generally results only in steady retrogression. In these 3 cases staphylococci, streptococci, and tubercle bacilli were the chief pathogenic organisms present. The technique of oral administration of the drug recommended by Marriott (1939) was adhered to as closely as possible. In all cases there was evidence of specific response to the drug, though in one case no such response had been made to sulphanilamide. The author concluded that sulphapyridine is specific in the control of this infection secondary to tuberculous empyema, but that its efficacy is limited to cases with an otherwise good prognosis.

Erwin, G. S. (1940) *Brit. J. Tuberc.*, **34**, 60

Marriott, H. L. (1939) *Brit. med. J.*, **2**, 944.

EMBOLISM, ARTERIAL

Treatment

Heparin

T. Olovson states that, in spite of the advances of the surgical treatment of arterial embolism, the results are still unsatisfactory. This is especially the case when a secondary thrombus has been formed. The formation of a secondary thrombus

is probably due to the combined effect of slow circulation behind the primary embolus and a lesion of the inner wall of the artery. The secondary thrombus may be of considerable length, and may make restitution impossible. The anticoagulant heparin is of considerable importance in the prevention of secondary thromboses. Heparin should be given intravenously before and after operation, and it may be used locally by injecting it into the wall of the artery after operation. Heparin should be used *before* operation or *before* conservative treatment, to save the peripheral parts of the artery and the collateral arteries. Its task is given after operation is to prevent secondary thrombosis. The dose is 2 to 3 c.cm. of a 5 per cent solution every 2 hours before operation, and 3 c.cm. every 4 hours after treatment. The stitching material used should also be heparinized.

Animal experiments have shown that heparin increases the amount of blood from a skin wound, but the bleeding stops after 10 minutes. Duration and intensity of bleeding is prolonged as against the normal.

Heparin was injected in experimental arteriotomy and the intensity of bleeding was increased; compressing and local application of viper venom, however, stopped the bleeding and the wound could be stitched. There was no after bleeding or formation of haematoma. No thrombosis was found in the operated arteries 2 to 8 weeks later.

Olovson, T. (1939) *Acta chirurg. scand.*, **82**, 487.

ENCEPHALITIS EPIDEMICA

See also B. E. M. P., Vol. IV, p. 546, Cumulative Supplement, Key No. 399, and Surveys and Abstracts 1939, p. 327.

Treatment

Parkinsonism and Psychosis

Benzedrine sulphate. L. Reznikoff studied the effects of benzedrine sulphate on 8 post-encephalitic patients suffering from psychosis and Parkinsonism. For the first two weeks of treatment the patients were given 10 mg. of the drug in 2 doses during the first half of the day. The dose was then increased to a total of 20 mg. After 4 months the patients were given placebos resembling the tablets of benzedrine. Some of the patients showed an occasional elevation of mood under treatment but they then became depressed and confused again and Reznikoff concluded that the drug made no significant change in the psychosis during the 4 months of treatment. Except that one patient became panicky on one occasion there were no untoward effects in this series. It was therefore concluded that the drug could be safely used for long periods provided the patient had no vascular disease or showed no idiosyncrasy to its use. Compared with atropine, stramonium, or scopolamine, drugs generally used in this condition, benzedrine was found to have no advantages except that it controlled oculogyric crises in 2 cases suffering from them.

Reznikoff, L. (1939) *Arch. Neurol. Psychiat.*, Chicago, **42**, 112.

ENCEPHALITIS HAEMORRHAGICA SUPERIOR

Wernicke's Disease

A. D. Ecker and H. W. Woltman reviewed cases of Wernicke's disease, or encephalitis haemorrhagica superior, all of which were associated with some endogenous or exogenous intoxication such as carcinoma or alcoholism. They reported a case occurring in a woman aged 50 years in which there was no evidence of intoxication, but evidence of dietary deficiency owing to inadequate nutrition. Since haemorrhages have been associated with vitamin-B₂ deficiency they suggested that all cases of Wernicke's disease might have an underlying vitamin deficiency as the cause. The woman had suffered from vomiting and on laparotomy a loop of ileum was found adherent to an old rectus scar. Six days after operation vomiting recurred and 8 days later mental confusion and restlessness were seen. Visual acuity then became less and the external ocular movements were limited. A number of large haemorrhages were seen in both retinæ. The patient lapsed into coma

with loss of tendon reflexes and died on the sixteenth day after operation. Necropsy showed typical haemorrhages in the mamillary bodies and posterior corpora quadrigemina. There were also a few petechiae elsewhere and atrophy of the liver and mucosa of the gastro-intestinal tract.

Ecker, A. D., and Woltman, H. W. (1939) *Proc. Mayo Clin.*, **14**, 520.

ENDOMETRIOSIS AND ADENOMYOMA

See also B.F.M.P., Vol. IV, p. 561, Cumulative Supplement, Key No. 401, and Surveys and Abstracts 1939, p. 329.

Clinical Aspects

M. I. Dreyfuss analysed 164 cases of adenomyosis uteri and 60 cases of endometriosis. Four per cent of the patients were under 35 years of age, and 96 per cent over 35 years, and 72 per cent over 40 years. Endometriosis occurs at the height of sexual life, whereas adenomyosis is commoner in the second half of the generative period. Endometriosis is often associated with sterility, whereas adenomyosis usually occurs in multiparae. Myomas are also present in about 70 per cent of cases with endometriosis. Hyperplasia of the endometrium or myomas were found in all cases of adenomyosis. Hypermenorrhoea and dysmenorrhoea were frequent in this condition, and if these occur between the ages of 35 and 50 years they suggest adenomyosis. Unfortunately they occur so often in other pelvic disorders that diagnosis is far from easy. Adenomyosis and endometriosis were combined in 6 cases only, and therefore probably have a different origin, although many of their manifestations are the same. Carcinomatous change is very rare in either condition.

Dreyfuss, M. I. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 95.

ENDOMETRITIS, CERVICITIS, AND METRITIS

See also B.F.M.P., Vol. IV, p. 574; Surveys and Abstracts 1939, p. 330, and p. 22 of this volume.

Endometrial Hyperplasia

Treatment

Progesterone. G. F. Seegar investigated the histological effect of progesterone on hyperplastic endometria. Seven cases were studied. In most of them a total of 50 mg. of progesterone was given, in 5 mg. doses over a period of 10 days. Endometrial biopsies were made before and after treatment. In 5 of the cases oestrogen and pregnanediol estimations were made on 48-hour specimens of urine before and after the injections. In only 2 cases was the progesterone recovered as pregnanediol, but in all but 2 cases the oestrogen value was normal.

Haemorrhage improved under the treatment in 6 patients, and in 4 of them, after treatment for several months, the menses became fairly normal. Progestational-like changes were produced in the endometrium even when the dose was too small for any of the progesterone to be recovered from the urine as pregnanediol. The substance was recovered from the urine when progestational changes were not present in the endometrium. According to Seegar 5 mg. was the smallest dose that would produce histological changes in endometrial hyperplasia, although a smaller dose might ameliorate the symptoms.

Seegar, G. F. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 469.

Cervicitis

Treatment

Coagulation and ionization. D. Derow describes a method of treating cervical erosion and endocervicitis which is claimed to be effective and to obviate most of the objectionable features of the methods at present in use. It is coagulation of the eroded areas of the cervix and lower end of the cervical canal for about $\frac{1}{2}$ inch with the bipolar high-frequency current, and coagulation of cysts, if any are present;

and copper-mercury or zinc-mercury ionization of the cervical canal. The method is safe, and there is little bleeding, and no stenosis of the cervical canal, and little or no pain. Of 210 patients treated, a follow-up of 180 showed complete relief of most of the local symptoms, such as leucorrhoea, painful menstruation, dyspareunia, irregular uterine haemorrhage, and bleeding after coitus. A few patients reported persistence of general symptoms, such as weakness, anorexia, and insomnia, but in a minor degree. In 12 cases only were there recurrences, and in each case this followed a pregnancy, subsequent to the treatment, a fact which indicates the definite relation of parturition to erosions and endocervicitis. Of 13 patients who attended chiefly for treatment of sterility, 8 became pregnant after treatment.

Solid carbon dioxide.—G. Weitzner treated 375 cases of endocervicitis with solid carbon dioxide with gratifying results. It was found that cases with erosion responded more readily to treatment. Of the cases, 75 per cent required only one application, 15 per cent required 2 treatments, and 15 per cent were treated 3 or more times. No post-operative sequelae such as bleeding, inflammation, or stenosis of the cervical canal were observed over a follow-up period of 2½ years, and no patient required hospitalization. Treatment is simple and painless: the area of destruction is limited, the inflammatory reaction is surprisingly little, and cicatrization is entirely absent. The technique of treatment is as follows. With the patient in the lithotomy position the vagina and cervix are wiped dry through a bi-valve speculum. No antiseptics and no anaesthetics are employed. A rod of solid carbon dioxide is made, large enough to fill the cervical canal. This is introduced into the entire length of the cervix with a uterine dressing forceps. A seething sound of vaporizing ice is heard, this ceases after 50 to 60 seconds, and this indicates the end of treatment. On withdrawing the ice pencil there is slight haemorrhage, if this does not occur, the procedure should at once be repeated. If an erosion is present, the ice should be pressed against it. Treatment should not be repeated more than once in 4 weeks. The after-treatment consists of inspection of the cervical canal once or twice a week, when tincture of iodine may be applied to the treated area. The patient should douche with hot alkaline solutions. If the ice breaks in the cervical canal, it should be allowed to melt in the cervix.

Novocain injection.—J. Figarella injected novocain, 1 in 200 solution, into the cervix uteri in endocervicitis. The usual dose employed was 20 to 25 c.cm. and this was injected into the submucous tissue of the cervix. Two treatments per week were generally given, and cure usually resulted after 4, 6, or 8 treatments. Treatment was begun immediately after a period. As a result of treatment pain quickly subsided, and leucorrhoea disappeared often after one injection. Erosions cleared up completely, generally after 5 or 6 treatments. Polypi disappeared after 4 or 5 injections. The fibrous type of lesion did not respond so well, and up to 10 treatments were necessary to obtain any real result.

Detow, D. (1940) *Arch. phys. Ther.*, **21**, 154.

Figarella, J. (1940) *Bull. Soc. Gyn. Obstet.*, **28**, 530.

Weitzner, G. (1940) *Amer. J. Surg.*, **48**, 620.

ENTERIC FEVERS

See also B.I.M.P., Vol. V, p. 50, and Surveys and Abstracts 1939, p. 330.

Typhoid Fever

Carriers

G. A. Soper gives a full account of 'the curious career of typhoid Mary' (Mallon), a cook, whom he discovered in 1907, and whose history he described when the existence of carriers was not widely recognized. In fact Mary may be said to be the first chronic typhoid carrier with infected faeces detected in America or other English-speaking countries. She was a masculine, irascible, pugnacious Irishwoman who denied having had typhoid and vigorously resented the suggestion that she spread typhoid. When she was found to be a carrier in 1907, she was imprisoned for two years and then brought an action against New York City under *habeas corpus* proceedings; but the Judge dismissed the case, saying that the court was

unwilling to take the responsibility of releasing her; nearly a year later she was allowed out of prison and disappeared for a time; but for the 23 years before her death in 1932 she had been segregated on North Brother Island. Soper traced to her agency 53 cases of typhoid fever with 3 deaths, dating from 1900. She was a nomadic cook who never stayed long in one place

Diagnosis and Differential Diagnosis

Isolation of bacteria from urine and faeces.—A. C. Ruys investigated the relative merits of various media for the isolation of pathogenic enteric bacteria from the urine and faeces. The media studied were those of Endo and Muller, those of Wilson and Blair (1931), Wilson (1933), Kauffmann (1931), Ruys (1934), and Leifson (1935). The conclusion reached was that, in cases of typhoid fever, the media of Wilson and Blair and of L. Muller are preferable, in paratyphoid B those of Muller and Ruys are best, and in the enteric form of the disease those of Kauffmann should be used. Endo's agar may give a positive result a day earlier than any of the others. Leifson's desoxycholate-citrate-agar and Endo's agar should be employed in bacillary dysentery.

Kauffmann, F. (1931) *Zbl. Bakt.*, **119**, 148.

Leifson, I. (1935) *J. Path. Bact.*, **40**, 581.

Muller, L. (1925) *C. R. Soc. Biol., Paris*, **93**, 433.

Ruys, A. C. (1934) *Zbl. Bakt.*, **132**, 349.

— (1940) *Brit. med. J.*, **1**, 606.

Soper, G. A. (1939) *Bull. N.Y. Acad. Med.*, 2nd ser., **15**, 698.

Wilson, W. J., and Blair, F. M. (1931) *J. Hyg., Camb.*, **31**, 138.

— (1933) *Brit. med. J.*, **2**, 560.

Treatment

Prophylaxis

H. Schutze showed that prophylactic inoculation during the incubation period of typhoid fever is not dangerous, as is often stated, but by analogy with the results obtained in mice is to be recommended during an epidemic in man. He experimented with mice infected with *S. typhi-murum* and 2 days later they were inoculated with a specific vaccine. The mortality-rate at the end of 3 weeks was 28 per cent, it being 41 per cent in a group of untreated control animals. The disease was no more severe than usual and the average length of life of the mouse was not decreased. Similarly, vaccination with specific vaccine after *S. enteritidis* did not accelerate the onset of the disease in mice.

Sulphapyridine

J. H. Stanyon records a single case of typhoid fever with a positive Widal and blood culture in a man, aged 24, with onset of symptoms on May 25, 1939. For 3 days when in hospital his temperature was between 102° and 104° F. Then, on June 3, he was given sulphapyridine (dagenan) 15 gr. and sodium bicarbonate 10 gr. every 4 hours, with the result that on June 6 his temperature became normal and remained so except for one rise to 99.2° F. The author employed sulphapyridine for want of more specific treatment and argued that, as such compounds exert a definite bacteriostatic and bactericidal action on *Bact. coli*, it is reasonable to expect a similar action on *B. typhosum*. The editor of the Journal adds a footnote pointing out that it should not be hastily concluded that sulphapyridine is a specific in typhoid fever, for there is evidence to the contrary. Further, typhoid fever has a tendency to cause leucopenia and so have sulphonamide drugs, so that caution and frequent blood counts are desirable, if such treatment is adopted.

Acute Confusional States

Adrenal cortical extract.—H. Hoff and J. A. Shaby reported on the use of adrenal cortical extract in acute confusional states. They stated that mental confusion in typhoid fever may occur in the first stage of the disease, when the prognosis is serious, or more commonly during convalescence. They reported 5 such cases, 2 in detail, which were successfully treated with adrenal cortical extract (cortigen) 2 c.cm. with vitamin C intravenously daily. They also treated 4 cases of mental confusion occurring during the puerperium after long and difficult labour. These

cases were also successful. The authors suggested that mental confusion may sometimes be due to hypofunction of the pituitary. The treatment failed in other cases of mental confusion of indefinite origin.

Carriers

Soluble iodophthalein.—W. Saphir and K. M. Howell, having found that a series of measures including the use of sulphanilamide failed to render the stools of a carrier of *B. paratyphosum* A free from this bacillus, employed soluble iodophthalein by mouth, in a dosage of 4 g. On the following day bacteriological examination of the stools failed to reveal the organisms. This dose of the dye was repeated twice in the next 6 days. Subsequent daily stool specimens remained negative for *B. paratyphosum* A. The dosage was continued once a week for 1 month, and the patient kept under observation for the following 7 months. Repeated examinations during this period were consistently negative. In vitro tests did not entirely explain this apparently antiseptic effect in the human carrier.

Hoff, H., and Shaby, J. A. (1940) *Lancet*, **1**, 27.

Saphir, W., and Howell, K. M. (1940) *J. Amer. med. Ass.*, **114**, 1988.

Schutze, H. (1939) *Lancet*, **2**, 643.

Stanyon, J. H. (1940) *Canad. med. Ass. J.*, **42**, 66.

EPIDIDYMITIS

See also B.E.M.P., Vol. V, p. 86.

Acute Epididymitis

Following Trauma

R. Fruhwald reported 9 cases in which epididymitis developed after trauma. Radiographic examination showed pathological changes in the prostate in 7 of these cases. Streak-like shadows were held to indicate dilated prostatic passages, and roundish shadows prostatic abscesses. The author considered that infection spread to the epididymis from these foci in the prostate, and that these cases proved that the true cause of non-specific types of epididymitis following trauma is to be found in inflammatory changes in the posterior urethra and adnexa.

Fruhwald, R. (1939) *Z. Urol.*, **33**, 650.

EPILEPSY

See also B.E.M.P., Vol. V, p. 96; Cumulative Supplement, Key Nos. 424-432, and Surveys and Abstracts 1939, pp. 124, 126 and 331.

Aetiology

R. B. Aird stated that the endothelium concerned with the formation of cerebrospinal fluid forms an effective protective barrier to the central nervous system. In animals with experimental epilepsy, brilliant vital red renders this 'barrier' relatively impermeable to the passage of cocaine hydrochloride. Brilliant vital red gives protection in cases of human epilepsy. This fact, in addition to various other considerations, affords strong evidence in support of the hypothesis that 'convulsive toxins' and the endothelium of the haemato-encephalic barrier are factors of aetiological importance in human epilepsy, and that the relation between them is analogous to that demonstrated in experimental epilepsy.

Aird, R. B. (1939) *Arch. Neurol. Psychiat., Chicago*, **42**, 700.

Treatment

Sodium Diphenylhydantoinate (epanutin)

O. P. Kimball and T. N. Horan consider that sodium diphenylhydantoinate is the most powerful anticonvulsant so far used. It has no tendency towards storage and is entirely eliminated from the body within 2 days. It does not impair memory or power of concentration, nor produce mental depression. In a series of 220 children and young adults, to whom this drug was administered for more than 6 months, the authors found complete control of the seizures in 55 per cent, partial control

in 20 per cent, and no effect in the remainder. The drug is effective in any type of epilepsy, including those cases in which convulsions were due originally to brain injury. Two unpleasant sequelae may occur from its use. In about 10 per cent of cases, a toxic rash, morbilliform in type and accompanied by some bronchitis may appear during the second week of treatment; and the sudden appearance of gastro-intestinal symptoms such as epigastric pain, with nausea or vomiting and even occasionally gastric haemorrhage.

R. Coope and R. G. R. Burrows employed sodium diphenylhydantoinate on 60 epileptic patients. The results were on the whole favourable, and often striking, in comparison with those obtained with other anticonvulsants. In 17 patients the total major attacks were reduced from 1,136 to 260 and the total minor attacks from 806 to 179. In substituting sodium diphenylhydantoinate for other drugs, the authors usually began with 0.1 g. the first day, then gave 0.2 g. the next, and 0.3 g. the next. On the fourth day a gradual reduction of the previously used drugs was begun, i.e., one of the 3 doses of a bromide mixture was omitted daily, then the dose of phenobarbitone, if any, was reduced by $\frac{1}{2}$ gram at a time until the patient was receiving the 0.3 g. of epanutin only. The process of substitution generally takes about a week. With this treatment there was improvement in the general physical and mental condition of the patient. Toxic symptoms, which were mainly mild, developed in 12 patients. Broncho-pneumonia caused the death of 2 patients after a condition approximating to status epilepticus, which appeared during treatment with the drug.

S. Davidson and J. D. Sutherland treated 12 chronic epileptic patients, some with psychotic behaviour, with sodium diphenylhydantoinate. The drug was given instead of sodium phenobarbitone or prominal to these patients, the latter drugs being gradually replaced by it. Nearly all the patients were over 40 years of age. Only one patient showed any mental improvement and this lasted for only a few weeks. The absence of sedative effect in the drug was undesirable in some patients as they became very irritable. On the whole the number of fits were slightly reduced by the epanutin but their character was not much changed. The most striking result of the treatment was the number of cases which showed toxic effects within a few weeks. These included nausea, loss of appetite, ataxia, and toxic rashes. The three youngest patients showed no toxic reactions. Davidson and Sutherland concluded that the drug is probably better used for younger or better-preserved patients. In the older more chronic cases it is better used only for a few weeks at a time as a useful addition to other drugs owing to its toxic effects.

J. L. Letterman also employed sodium diphenylhydantoinate in the treatment of 28 cases of epilepsy, over a period of 11 months. The dosage was 0.1 to 0.2 g., 3 times a day; at first the previous medication was replaced fairly promptly, but later the substitution was made more gradually, over a period of 3 weeks. In at least 10 cases the therapeutic results were excellent, the patients becoming free from attacks or the seizures being greatly reduced even when previous treatment with other remedies had given little or no benefit. In 2 cases the improvement was moderate and in 3 fair. In 4 cases there was a reduction in the attacks, but this good therapeutic response was mostly offset by uncomfortable side-effects of the drug. Side-effects comprised neurological symptoms, negative and nervous reactions, and psychic disturbances. The neurological symptoms consisted of tremors and ataxia, and less frequently blurring of vision, loss of taste, and dysaesthesia in the mouth. Nervous reactions included restlessness. Psychic disturbances included insomnia, irritability, suspiciousness and quarrelsomeness. Other side-effects in some cases were a slight dermatitis, swelling and puffiness of the gums, and anorexia, gastric distress, and loss of weight. A striking difference between the actions of the drug and phenobarbitone was that, whereas the latter was soothing and relaxing, and even depressing, to most patients, sodium diphenylhydantoinate tended to produce alertness and wakefulness. For patients who are drowsy with phenobarbitone, and for those with occasional and infrequent attacks, the author considered that phenobarbitone was preferable, for those not benefited by the latter, sodium diphenylhydantoinate should be tried. It was found that the disturbing side-effects generally grew milder in the course of time. The drug should be employed only under the careful supervision of the physician.

A. J. M. Butler employed sodium diphenylhydantoinate in 43 cases of epilepsy. In

most cases the drug was given in place of phenobarbitone or prominal; in some cases the patients had been having, in addition, mixtures containing bromides, belladonna, chloral hydrate, etc. With regard to the incidence of fits, great improvement was obtained in 20 cases (46.51 per cent), improvement in 7 cases (16.28 per cent), and no change in 6 (13.96 per cent), 1 case became worse, and in 9 cases treatment was discontinued. In the case in which treatment was discontinued various toxic symptoms and signs had occurred; such manifestations included pyrexia, skin rashes, hypertrophic gingivitis, nausea, vomiting, tremulousness, intention tremor, ataxic gait, nystagmus, ptosis, slurring speech, insomnia, and mental confusion. Most of these toxic effects disappeared within a few days after cessation of treatment. The patients' ages ranged from 17 to 58. The impression was gained that patients of low-grade mentality were less likely to derive benefit and were more likely to exhibit toxicity than those nearer average intelligence.

D. Williams treated 91 chronic epileptics with sodium diphenylhydantoinate. These patients had been closely followed for many years and their condition had not been greatly affected by any other form of treatment. They were given a daily dose of 0.2 g. or 0.3 g., slowly increasing to 0.6 g. daily in some cases. The period of treatment varied from 10 months to 6 weeks, the average duration in 83 cases being 4.1 months. Of patients with major epilepsy 79.1 per cent and of those with minor epilepsy 62.8 per cent were benefited by the treatment; 19 per cent showed a dramatic and maintained improvement. In some cases there was no improvement until the dose was increased from 0.2 or 0.3 g. daily to 0.4 g. Any patient receiving 0.5 g. or more daily developed toxic symptoms. In 8 patients, although the number of fits was reduced, they increased in severity or changed in character. Two such patients died in status epilepticus when receiving 0.5 g. and 0.4 g. daily. In 36 per cent of the patients toxic, nervous, mental or alimentary symptoms developed. Williams concluded that the drug was valuable in the treatment of some cases of epilepsy but that owing to its toxic reactions it must be used with care. He thought that it should not be substituted for the less toxic anticonvulsants in the initial stages of treatment.

Hemiplegia following treatment—D. Blair described a case of idiopathic epilepsy with psychosis. The patient, a woman of 34, was freed completely from fits which had numbered about 15 a day, by sodium diphenylhydantoinate (epanutin), 1 capsule thrice daily. After 6 months of freedom the fits recommenced. The dosage of the drug was first increased, then the drug was withdrawn. The fits reached 26 in 1 day. They were then controlled by the intravenous injection of evipan. After this the patient was found to have a right-sided hemiplegia which cleared up in the course of a few days. Blair concluded that the hemiplegia was due directly or indirectly to the sodium diphenylhydantoinate, but gave no evidence for this assertion.

Phenobarbitone

Effect on mentality—F. Somerfeld-Ziskind and F. Ziskind investigated the effect of phenobarbitone on the mentality of 48 epileptic patients; 42 similar patients were studied as controls. Before treatment the intelligence quotient was studied by various methods. The average for this series was 93, 100 being the accepted average for normal persons. Memory, attention, and language ability were the most often found deficient mental traits. Reaction time in free association tests was slower than in normal persons. The treated patients received 1 to 3 doses of phenobarbitone daily for 1 year. The average total daily dose varied from $\frac{1}{2}$ gr. to 4 $\frac{1}{2}$ gr. After 1 month's treatment the differences in mentality between the treated and control groups were very slight. After 1 year's treatment the mental age of those less than 16 years old, which might be expected to increase, increased more in the treated than the control group. There were no significant changes in the time reaction to free association. The intelligence quotient showed no deterioration in either group. After 2 years' treatment 7 patients showed, if anything, slightly improved mentality. Treated patients, however, showed a marked reduction in the number of fits. The authors therefore concluded that phenobarbitone is a good sedative in the treatment of epilepsy and given in doses of 1 $\frac{1}{2}$ gr. 2 or 3 times a day does not produce any deterioration of the intellect.

Comparative Effects of Phenobarbitone and Sodium Diphenylhydantoinate

B. Cohen *et al.* described the results of treatment of epileptics with phenobarbitone, sodium diphenylhydantoinate, and other drugs. It was found that the increase of phenobarbitone up to an average of 3 gr. per day per patient, with due regard for the individual effect, was attended by a great reduction in the incidence of attacks, amounting to about 68 per cent when compared with treatment by phenobarbitone alone, given in a routine manner and haphazardly. Sodium diphenylhydantoinate alone did not exert as favourable an effect in cutting down attacks as adequate doses of phenobarbitone. The use of benzedrine was recommended because of its value in dissipating the effect of idiosyncrasy or excessive doses of phenobarbitone. It also exerted a favourable, though somewhat less marked, effect on the toxic manifestations of sodium diphenylhydantoinate, and it permitted these drugs, especially phenobarbitone, to be continued in unchanged doses, even when such dosage by itself produced untoward results and when the reduction of dosage would result in increased attacks. A combination of phenobarbitone and sodium diphenylhydantoinate was found to be far more efficient than either drug alone, the reduction in the number of attacks being at least 50 per cent greater than the most favourable results obtained without the synergistic use of these drugs.

L. J. Robinson and R. Osgood also investigated the comparative effects of phenobarbitone and sodium diphenylhydantoinate in the treatment of epilepsy. The effect of these drugs was evaluated on the basis of effect on seizures, salutary effects, effects on the general condition of the patient, and untoward effects. One hundred patients were treated with phenobarbitone, the maximal and optimal doses ranging from 3½ to 11½ gr. a day. Fifty-six patients who were not greatly benefited by large doses of phenobarbitone were given sodium diphenylhydantoinate in gradually increasing doses, ranging from 3 to 13½ gr. Several patients derived no appreciable beneficial effect from these drugs, and some were intolerant to relatively small doses of either drug. In some of these cases a combination of the two drugs gave remarkably good results.

Prominal

C. G. Millman reports on 5 years' routine treatment of epilepsy by prominal, a methyl derivative of phenobarbitone. The treatment was given to 154 epileptics of both sexes and all ages, ranging mentally from the idiot to the high-grade feeble-minded. Among these there were 23 deaths, some in aged and debilitated patients. But 2 patients died from uraemia, and since then the urine of all patients taking prominal has been tested, and albuminuria has been the signal for suspension of this treatment. The results were good in the majority of the 154 cases and excellent in some, but disappointing in 25. Prominal is superior to phenobarbitone in the control of fits and non-convulsive manifestations of most of the cases, and is less hypnotic. The drug did not lose its power when given for 5 years except in a small number of the patients.

Insulin-free Pancreatic Extract

C. Rouvroy employed deinsulinized pancreatic extract in 5 cases of minor epilepsy. He found that this preparation shortened the duration of attacks of minor epilepsy, and relieved secondary phenomena such as excitement, agitation, hallucination, and refusal of food. The author stated that the extract was effective in cases in which other potent agents, such as barbiturates, were unsuccessful. In 2 cases of major epilepsy the duration of intermittent attacks was shortened.

Blair, D. (1940) *Lancet*, **1**, 269.

Butler, A. J. M. (1940) *Brit. med. J.*, **1**, 483.

Cohen, B., Showstack, N., and Myerson, A. (1940) *J. Amer. med. Ass.*, **114**, 480.

Coope, R., and Burrows, R. G. R. (1940) *Lancet*, **1**, 490.

Davidson, S., and Sutherland, J. D. (1939) *Brit. med. J.*, **2**, 720.

Fetterman, J. L. (1940) *J. Amer. med. Ass.*, **114**, 396.

Kimball, O. P., and Horan, T. N. (1939) *Ann. intern. Med.*, **13**, 787.

Millman, C. G. (1939) *J. ment. Sci.*, **85**, 970.

- Robinson, L. J., and Osgood, R. (1940) *J. Amer. med. Ass.*, **114**, 1334.
 Rouvroy, C. (1939) *J. belge Neurol. Psychiat.*, **39**, 676.
 Somerfeld-Ziskind, F., and Ziskind, L. (1940) *Arch. Neurol. Psychiat. Chicago*, **43**, 70.
 Williams, D. (1939) *Lancet*, **2**, 678

In Children

Treatment

Encephalographiv.—According to T. Schleier encephalography produces a good therapeutic effect on epilepsy. The quantity of air insufflated has no special effect on the result. Considerable trouble resulting from insufflation probably indicates a good prognosis. The therapeutic effect diminishes at puberty. The interval between the first attack and encephalography is unimportant for therapeutic effect.

Schleier, T. (1940) *Arch. Psychiat. Nervenkr.*, **111**, 200

Myoclonus Epilepsy

Associated with Primary Optic Atrophy

M. P. Rosenblum and M. Herman state that, in 1,224 cases of epilepsy admitted to Bellevue Hospital, New York, myoclonus epilepsy occurred twice only. The myoclonus is progressive and may occur before, with, or after the fits begin. The myoclonic contractions are more common in the arms and shoulders, but there may be a generalized status myoclonus. It is a degenerative familial disease, involving the dentate system, the basal ganglia, the midbrain, and often the cortex. Extrapyramidal symptoms result from the involvement of the basal ganglia. A case is reported in a man, aged 35, complicated by primary optic atrophy, the other cranial nerves being normal. The patient had his first fit in the first year of life and shortly afterwards began to have twitchings of the body. When seen he showed generalized myoclonic contractions and mental and emotional deterioration. Vision was reduced to counting fingers at 1 foot. There was no abnormality in X-ray examination of the skull or in examination of the urine or cerebrospinal fluid. There was no positive family history for either epilepsy or myoclonia.

Rosenblum, M. P., and Herman, M. (1940) *J. nerv. ment. Dis.*, **91**, 456

EPILOIA

See also B.F.M.P., Vol. V, p. 117

Bone Changes

G. S. Hall records 2 cases of the rare condition of bone lesions in tuberous sclerosis (epiloia), and discusses the nature of the changes which differed in the 2 cases. In a man, aged 34 years, of average intelligence, who had never had fits, there was a history of bilateral (internal ear) deafness from the age of 17, the Balzer type of adenoma sebaceum was profuse on the face, and elsewhere there were small tumours, especially on the hands and feet. Radiologically, the skull showed areas of increased density in the frontal bone, and both petrous bones were unusually dense and massive, the internal auditory meatus on each side being thus obscured. The ulnae were broadened along their whole length and rarefied in the upper third, suggesting fibrocystic changes. All the bones of the hands were somewhat broadened, and some of the phalanges showed rarefaction also suggesting cyst formation. These lesions resemble those that may occur in neurofibromatosis. In the other case, a boy aged 16 years, who had been subject to fits since 7 months of age, to the skin condition since the age of 1 year, and was slightly subnormal mentally, the bony changes were quite different and, unlike those in the first patient, have not been previously described in epiloia, in the right hand the proximal half of the thumb was enlarged to form a hard nodular swelling on its ventral aspect, the forefinger considerably broadened and very nodular, the proximal third of the middle finger a little expanded, whereas the 2 inner fingers, particularly the ring finger, were unusually thin and tapering; the other hand did not show any such changes. The lesions are identified with those of rheostosis, a congenital developmental abnormality. The association of epiloia with neurofibromatosis and

rheostosis is explained on the basis that all 3 conditions are members of the group of 'the development tissue dysplasias' described by Parkes Weber.

Hall, G. S. (1940) *Quart. J. Med.*, **9**, 1.

Weber, F. P. (1939) *Proc. R. Soc. Med.*, **32**, 440.

EPIPHYSES, DISEASES AND INJURIES

See also B I M P., Vol. V, p. 127, and Surveys and Abstracts 1939, p. 334.

Perthes' Disease

W. Muller and W. Ioepp published their observations on Perthes' disease. They found that the disease occurs in the third or fourth year of life though fragmentation could not be found in the radiographs. The characteristic X-ray appearance of this early stage is, according to the authors, a rarefaction in the head of the femur near the junction of the cartilage. They are of the opinion that the cartilage invades the atrophic spongiosa, in a manner similar to the vertebral invasion of cartilaginous nodules in Schmorl's syndrome. The early bone changes are only temporary and often disappear before diagnosis can be made.

Muller, W., and Ioepp, W. (1939) *Fortschr. Röntgenstr.*, **60**, 294.

Epiphysitis

Regeneration of Epiphyseal Centres of Ossification

S. W. Banks *et al.* report 5 cases of epiphysitis due to pyogenic or tuberculous infections, in which the centres of ossification later regenerated. The power of regeneration depends upon the amount of cartilaginous tissue escaping destruction. Longitudinal growth of the shaft of the bone takes place through what is left of the cartilaginous epiphyseal plate. In 1 case the centre of ossification at the lower end of the femur was completely destroyed and growth of the shaft ceased. When the centre regenerated, the shaft began to grow again. In another case most of the epiphysis of the head of the femur was necrosed or removed, but at operation most of the cartilage was found to be present; this led to regeneration of centres of ossification and satisfactory growth of the bone.

Banks, S. W., Krugsten, W., and Compere, F. L. (1940) *J. Amer. med. Ass.*, **114**, 23.

Epiphysitis of Spine

L. Nathan and J. G. Kuhns review the clinical and radiographic manifestations in 75 cases of epiphysitis of the spine. The disease is most often seen in rapidly growing children. In 14 patients there was a family history of similar spinal disease. X-rays showed irregularity of the upper and lower surfaces of the vertebral bodies to be the most constant lesion. Decalcification of the vertebrae was observed in 8 patients only. The so-called Schmorl's islands were seen in 21 cases. The late change was constantly an anterior wedging of the vertebral body. All degrees of severity of the lesion were observed. The deformity decreased with, but was rarely corrected by, treatment. In 2 cases deformity was absent. Treatment in most cases consisted in the application of a plaster jacket with the spine in extension, and corrective exercises. Recumbency in a plaster shell with the thoracic spine in extension—as carried out in 5 cases—seemed to be the most efficient form of treatment. In adults who had not received any treatment, severe deformity was generally present, and was usually associated with pain and weakness in the back.

Nathan, L., and Kuhns, J. G. (1940) *J. Bone Jr Surg.*, **22**, 55.

Osteochondritis

Apophysitis of Acromion

E. N. Cleaves reports a case regarded as osteochondritis of the apophyses of the acromion of the scapulae. A young man, aged 17, fell on his right elbow, but felt pain in the shoulder. Radiography showed absence of fracture and dislocation, but changes in the apophyses of both the acromions. The apophyses were smaller than normal, irregular in shape, and of increased density. The patient's signs and

symptoms gradually subsided and, 16 months later, radiologically the apophyses of the acromion were still smaller than normal, slightly irregular, and somewhat less dense than normal. They were, however, definitely assuming the appearance of normal bone. The epiphyseal lines were still partly open, but gave evidence of beginning closure.

Cleaves, I. N. (1940) *J. Bone Jt Surg.*, **22**, 182

ERYSIPELAS

See also B.F.M.P., Vol. V, p. 154, and Surveys and Abstracts 1939, p. 335

Prognosis

A. L. Hoyne *et al.* analyse the mortality rates in various forms of treatment of erysipelas in 998 patients. In 1938, among 141 patients, the mortality was 2.1 per cent. The disease was most often fatal in the very young, the old, and surgical and debilitated patients. Death is commoner in males than females. The part of the body affected influences the prognosis. In its most severe form it is commonest around the nose and ears. Several forms of treatment were used, including ultra-violet rays and convalescent serum. Sulphanilamide and its derivatives gave the best results. Among 162 patients so treated the mortality was only 2.46 per cent whereas in 477 cases receiving ultra-violet light it was 10.9 per cent.

Hoyne, A. L., Wolf, A. A., and Prim, I. (1939) *J. Amer. med. Ass.*, **113**, 2279

Treatment

Sulphanilamide

I. A. Rantz and C. S. Keefer employed sulphanilamide in 42 cases of facial erysipelas. The dosage was 6 to 8 g. in the first 24 hours, followed by maintenance doses of 3 to 5 g. daily. Successful results were obtained if therapy was commenced on or before the third day of illness, the average length of pyrexia in such cases being 5.2 days, as opposed to 7.5 days in the untreated. But, in cases where sulphanilamide was given after the third day, the duration of pyrexia averaged 9.1 days, or substantially longer than that experienced in the untreated group. The incidence of complications tended to be reduced after early sulphanilamide administration, but there was no more freedom from relapses or recurrences than was found in the untreated class.

Rantz, I. A., and Keefer, C. S. (1939) *New Engl. J. Med.* **221**, 809

ERYTHRAEMIA

See also B.F.M.P., Vol. V, p. 176, and Surveys and Abstracts 1939, p. 336

Radiological Changes in the Lungs

Eight out of 11 patients with erythraemia showed radiologically much increase in the prominence of the truncal shadows in the lungs, and 3 patients in addition presented circumscribed nodular lesions ascribed to stasis infarction. Three patients with secondary polycythaemia due to pulmonary arteriosclerosis did not present the above changes, but showed well-marked prominence of the hila, increased prominence of the pulmonary conus, and hypertrophy of the right heart. P. J. Hodes and J. Q. Griffith undertook these observations in order to determine any diagnostic difference between erythraemia and secondary polycythaemia.

Hodes, P. J., and Griffith, J. Q. (1939) *Trans. Coll. Phys. Philad.*, 4 ser. **7**, 261.

EYELIDS, INJURIES AND DISEASES

See also B.E.M.P., Vol. V, p. 239, and Surveys and Abstracts 1939, p. 338

Mycetoma

J. S. Aldridge and R. Kirk record mycetoma of the eyelid in a girl of 4 years of age. There was a mass about the size of a marble at the outer angle of the upper eyelid, and passing up under the orbital ridge. The swelling was more prominent on the skin than on the conjunctival surface. There was no tenderness. The overlying skin was normal, and not attached to the mass. Histological examination of sections of the tissue from the swelling established the diagnosis of mycetoma.

Aldridge, J. S. and Kirk, R. (1940) *Brit. J. Ophthalmol.*, **24**, 211

Molluscum Contagiosum of Eyelid and Cornea

T. H. Quill describes a case in a girl, aged 13, with molluscum contagiosum involving the right lower eyelid, thickening of the conjunctiva of both lids, and a zone of vascularized overgrowth of tissue 3 to 5 mm. wide extending over the periphery of the cornea. Excision of the lesions from the cornea and lid was followed by distant vision of 6/10 as compared with perception of hand movements at 1 metre before the operation. Molluscum contagiosum of the eyelids is rare; among 128 cases in various parts of the body, seen at the Mayo Clinic, there were 10 other cases in which the eyelids were affected, but in none of these was the conjunctiva involved. Elschnig is quoted as having reported 4 examples of involvement of the eyelids among 10,000 ophthalmic cases at Prague.

Elschnig, A. (1922) *Arch. Ophthalmol.*, N.Y., **51**, 237

Quill, T. H. (1940) *Proc. Mayo Clin.*, **15**, 139

Tumours*Schwannoma*

R. Argaud and L. Calmettes describe a very rare case of tumour of Schwann's membrane. Most nervous tumours of the eyelids are plexiform neuromas, constituted by a hypertrophy or hyperplasia of nervous fibres and their membranes. The case described by the authors was a schwannoma nearly exclusively formed by plasmodial hyperplasia. The tumour was semi-soft, not painful, and had not caused any inflammatory reaction. There were no other pathological manifestations. Microscopical examination after excision showed signs rather of a hyperplasia with palisade formation of nuclei and secondary filling of the plasmodial space with fibrils which is a picture typical of schwannoma.

Argaud, R., and Calmettes, L. (1939) *Arch. Ophthalmol., Paris*, **3**, 690.

FALLOPIAN TUBES DISEASES

See also B.E.M.P., Vol. V, p. 250, Surveys and Abstracts 1939, p. 338; and p. 23 of this volume

Non-Patency*Treatment*

Follicular hormone.—M. Moore White reported the results obtained with follicular hormone in 13 cases of non-patent or only slightly patent Fallopian tubes. Clauberg (1938) introduced the method, on the hypothesis that oestrin stimulation induces hyperaemia, and hence increased development with expansion of the tube. White employed in these cases a course of 5 injections of 50,000 I.B.U. at 5-day intervals. Four of the 7 cases, in which non-patency of the Fallopian tubes was confirmed both

by radiographs and by insufflation acquired patent tubes, with good tubal contractions in 3 cases, and poor contractions in 1 case. Three of these women became pregnant, 2 miscarrying at 6 weeks. Of 2 cases in which the tubes were shown to be non-patent on insufflation only, patency and good contractions resulted in 1 case. Of 4 cases in which the tubes were patent only at high pressure and showed no tubal contractions, 3 subsequently became patent at a lower pressure and showed tubal contractions. In 2 of the cases in which patency resulted and good tubal contractions were obtained, examination of the husband's semen showed a poor spermatozoa count, below the standard for successful impregnation. The author also reported the results obtained in 65 cases of sterility by lipiodol (iodized oil) injections in conjunction with endocrine therapy. In 26 per cent of the cases pregnancy resulted.

Clauberg, C. (1938) *Zbl. Gynak.*, **62**, 1034.

White, M. M. (1940) *Brit. med. J.*, **1**, 342.

FLVER THERAPY

Cerebral Hydrodynamics

O. T. Wood and A. McCravey investigated the cerebral hydrodynamics in 4 cases of fever therapy, in which a total of 12 treatments had been given, extreme states of cerebral anoxia and hyperaemia occur, and can be recognized clinically. The chief feature is the dramatic clinical change produced by disturbance of intracranial volume-pressure relationships. The pulse pressure is the best clinical index for determining the state of cerebral circulation. Cerebral anoxia can be relieved by properly timed and sufficient removal of cerebrospinal fluid. Cerebral hyperaemia could be prevented by insufficiently stabilizing intracranial volume-pressure relationships.

Wood, O. T., and McCravey, A. (1940) *J. Amer. med. Ass.*, **114**, 1437.

FIBROSITIS

See also B.E.M.P., Vol. V, p. 279, and Cumulative Supplement, Key No. 489

Clinical Picture

M. Gutstein defined common rheumatism as a disease giving rise to severe pain in the soft tissues covering the body or in the joints, exclusive of pain caused by inflammation or injury, or neuralgia. This condition is synonymous with so-called fibrositis, a bad term since there is no evidence that it is due to inflammation. The author suggested rheumatic myalgia as a better name for the condition, the cause of which is unknown. The pain is a referred pain, referred from myalgic spots, the exact location of which is of the greatest importance in treatment. Any muscle may be affected but some, such as the trapezoid and quadratus lumborum, are more commonly concerned. The pain is dull, occurs in attacks, and is often accompanied by paraesthesia. Examination shows that the myalgic spots always correspond to anatomical points, namely the origin, insertion, or course of a muscle or its tendon. Palpation over these spots elicits a sharp pain and the tissues feel thicker than normal. A nodule may or may not be felt. Trauma, deficient circulation, endocrine deficiency, septic foci, an upset in blood-chemistry, and allergy may all play a part in the aetiology of rheumatism. General treatment should include the eradication of any of these factors if they are present, and the establishment of a vegetarian diet for a fortnight. Gutstein has had very good results from the local application of infra-red rays to the myalgic spots combined with massage. He considered that all cases of common rheumatism can be cured by this means in a short time and he reported 3 illustrative cases.

Gutstein, M. (1940) *Brit. J. phys. Med.*, **3**, 46.

Treatment*Cobra Venom*

O Steinbrocker *et al* report on the use of cobra-venom extract in arthralgias and related conditions in 65 patients, almost all of whom had not obtained adequate relief from other kinds of therapy. Some of the patients were placed on cobra-venom therapy at once, others were given a course of physiological solution of sodium chloride to serve as a control. The treatment of some of the patients receiving cobra venom and showing improvement was interrupted without their knowledge, and physiological solution of sodium chloride was substituted to determine the veracity of the previous response. The cobra venom was given at first in doses of 1 c cm (5 mouse units) daily or every second day, by intramuscular injection. This dosage proving too mild in arthritic conditions, it was increased to 2 c cm. Ten injections, or 50 mouse units, were considered to be the minimal standard trial series for eliciting any notable clinical effect. When improvement persisted during a period of 3 or 4 injections, the dose was reduced or the interval between injections was gradually lengthened. Of the patients given saline solution, 7 (19.4 per cent) showed slight to moderate relief, and of those receiving venom 36 (59.01 per cent) were slightly or moderately benefited. In this preliminary investigation a small but suggestive group, particularly those with arthralgias, experienced some gradual, but rarely complete, relief of pain and, in a smaller number of cases, improved mobility, during the treatment. There was on the whole some limited efficacy of cobra venom as compared with controls treated with saline. Cobra venom appears to offer some supplementary analgesic effect to tide patients over an intractable period of treatment in acute or chronic arthralgia or neuralgia.

Steinbrocker, O., McEachern, G. C., La Motta, I. P., and Brooks, F. (1940)
J. Amer. med. Ass., **114**, 318.

Bursitis*Epicondylitis*

Sodium morrhuate therapy—I. A. Slowick employed sodium morrhuate injections in 5 cases of epicondylitis of the humerus, or radio-humeral bursitis with successful results. There was no evidence of subcutaneous-tissue damage. Following the injection of novocaine subcutaneously, 0.3 c cm. of a 5 per cent solution of sodium morrhuate was injected beneath the extensor tendon at its attachment to the epicondyle. There was generally a temporary aggravation of symptoms. Some days later a further injection of 0.3 c cm. was given. In 1 case only was a third injection necessary to clear up the symptoms.

Acute Acromial Bursitis

Surgical treatment—W. P. Bartels treated 33 cases of acute acromial bursitis by open operation, and considered that surgical treatment offered a more prompt and certain cure of the condition than medical treatment. X-ray examination showed calcified deposits about the tuberosities of the humerus in 90 per cent of cases. Surgical treatment is followed by relief from severe pain within 24 hours, and return of from 60 to 90 per cent of function of the shoulder and extremity at the end of 3 weeks. The operation is simple and takes from 15 to 25 minutes under general anaesthesia. A three-inch incision, from the anterior edge of the acromion downwards is made. The deltoid is split in the direction of its fibres. The oedematous roof and walls of the subacromial bursa are dissected out and excised. Cloudy fluid and, infrequently, a calcified plaque, may be found in the bursa. The tendons of insertion of the supraspinatus, infraspinatus, and teres major are examined for calcified deposits by making small incisions in the direction of the tendon fibres. Thorough removal of all calcified material is essential, and this is effected by a curette; this is followed by sharp incision of infiltrated tendon fibres. No sutures are needed to close the small incisions in the tendons. The deltoid muscle is loosely approximated, and the skin closed with interrupted sutures, so placed as to allow seepage from the wound for 12 hours after the operation. No splint or retentive device is used.

Bartels, W. P. (1940) *J. Bone Jt. Surg.*, **22**, 120.

Slowick, I. A. (1940) *New Engl. J. Med.*, **222**, 1071.

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

See also B.E.M.P., Vol. V, p. 334; Cumulative Supplement, Key Nos 503-512, and Surveys and Abstracts 1939, p. 340.

Abnormalities in Living Foetus

Skin

Ehlers-Danlos disease —J. E. Murray and M. L. Tyars describe in a man, aged 28, the syndrome recorded in 1901 by Ehlers and in 1908 by Danlos. The features of this condition are (1) abnormal elasticity of the skin, (2) friability of the skin and blood-vessels so that large subcutaneous haematomas and gaping wounds may follow trivial injuries, (3) hyperextensibility of the joints, (4) papyraceous scars, sometimes associated with pseudo-tumours, (5) tiny movable nodules, probably of fat, and (6) a familial incidence of one or more of these constituents. The authors did not find any reference to the familial incidence in American or British publications, but they give a pedigree showing that their patient's father and 2 of his 3 sisters and his only brother were affected, all the affected members of the family showed the condition from the age of 3 to 4 years or even earlier. Although regarded as extremely rare, it is suggested that many of the elastic men and contortionists in side-shows may be the subjects of this disease which thus provides them with a source of profit.

Arachnodactyly

J. J. Fahey reports 6 cases of arachnodactyly. In 2 of them muscle was examined microscopically but no abnormality was found. X-ray examination showed the slender bones in the affected parts and the decrease in the soft tissues. The condition is often familial, transmitted by either sex, and its cause is unknown. The soft tissue of the body is always decreased in some part, particularly in the extremities. It has been suggested that the condition may be a primary muscular dystrophy. Relaxation of the ligaments, especially in the hands and feet, is usually present. Contractures, especially of the fingers, commonly occur. The hands and feet are often longer than in normal persons. The patients are usually tall, and there may be deformities of the spine, head, and chest. About 35 per cent of the patients show some cardiac lesion, sometimes congenital. Ocular lesions, such as dislocation of the lens and myopia, are common.

Congenital Arteriovenous Fistula

J. C. Luke records 3 cases and reviews the condition of congenital arteriovenous fistula (or communication), the cause of which, unlike the acquired or traumatic examples, is obscure. Until recently the congenital form was unrecognized, because its manifestations were so numerous and passed under different names, such as cirsoid and racemoid aneurysm, phlebarteriectasis, haemangiectatic hypertrophy (Parkes Weber's syndrome), angioma arteriale, glomus tumour, and congenital hypertrophy of a limb. When the communication is large, the systolic pressure is low and the arterial wall thinned, 'ventilation', the vein wall becomes thickened, 'arterization.' The blood is returned to the heart sooner than normal, and cardiac failure may result from increased work. Bragman's sign depends on these altered conditions: it is positive when the pulse rate falls 10 to 20 beats a minute when the artery is obliterated proximal to the arteriovenous communication.

Fahey, J. J. (1939) *Arch. Surg., Chicago*, **39**, 741.

Luke, J. C. (1940) *Canad. med. Ass. J.*, **42**, 341.

Murray, J. E., and Tyars, M. E. (1940) *Brit. med. J.*, **1**, 974.

FOOD

See also B.E.M.P., Vol. V, p. 388; and Surveys and Abstracts 1939, p. 341.

Malnutrition

Danger of Forcing Fluids

J. A. Evans and H. Shulman report 4 cases showing the danger of forcing fluids

in malnutrition. Massive oedema may be produced by this means, and one of their patients died of pulmonary oedema. Another patient with Addison's disease died after eclamptic-like convulsions. Many believe that eclampsia of pregnancy is due to fluid imbalance and hypoproteinaemia; both states can be induced by excessive fluids. Although the patient is dehydrated in malnutrition, because hypoproteinaemia is present it is unwise to give large quantities of salt and water intravenously. The authors believe that a low fluid output is a better indication of dehydration than a dry tongue.

Evans, J. A., and Shulman, H. (1940) *Amer. J. med. Sci.*, **199**, 237.

FOOT. DISEASES AND DEFORMITIES

See also B L M P, Vol V, p 412, and Surveys and Abstracts 1939, p 342

Acquired Deformities

Hallux Valgus

Method for control of post-operative pain.—M. H. Bloomberg described a method which minimizes the pain after operation for hallux valgus, allows movement to be instituted much earlier than usual, definitely shortens the period of disability, and may obviate the occurrence of hallux rigidus. The method consists in crushing the sensory branches innervating the region, and thus producing temporary anaesthesia, which lasts for about 8 weeks, during which period care is taken to avoid pressure on the anaesthetized area. After anaesthetizing with 0.5 per cent procaine hydrochloride and adrenaline solution, the joint is exposed by a curved dorsi-medial incision. The superficial layers are dissected backward and laterally. The medial and lateral dorsal digital nerves are isolated and crushed with a haemostat for a distance of 1 cm. Care is necessary so as not to sever them. After reconstruction of the joint and closure of the wound, the toe is placed in a splint, and strongly abducted by a pad between the first and second digits. Wide shoes must be worn until sensation returns, so as to avoid pressure sores.

Bloomberg, M. H. (1940) *Amer. J. Surg.*, **48**, 412.

Tumours

Primary Tumours of Hands and Feet

G. T. Pack *et al.* contribute 5 articles on tumours of the hands and feet, carcinoma, subungual melanoma, angiomas, tumours of the synovia, tendons, and joint capsules, and primary tumours of the bones. Pack, who edited this symposium, supplies a general introduction, emphasizing the special characteristics of new growths in the hands and feet, such as their liability to attract early attention, multiplicity of these tumours, malignant as well as benign, and the fact that they should all be prevented. Full use was made of the experience of the Memorial Hospital for Cancer and Allied Diseases, New York, where during the 21 years 1917-38 there were 573 tumours (369 malignant, 204 benign) of the hands and feet, the hand being affected more often than the feet. The radio-sensitive benign tumours are warts, epithelial papillomas, angiomas, and granulomas; and of malignant growths epidermoid carcinomas, basal-celled carcinomas, Kaposi's sarcoma, and endothelial myeloma (Ewing's tumour); all the other tumours are radio-resistant. In the group of malignant tumours irradiation treatment should never supplant surgical excision or amputation as the sole method of treatment of osteosarcoma, malignant melanoma, spindle-celled sarcoma and myxosarcoma of undetermined histogenesis. Although Ewing's tumour rapidly diminishes under irradiation, this usually fails to bring about a permanent cure, and it is therefore advisable to follow such irradiation by amputation. As the idiopathic haemorrhagic sarcoma of Kaposi is of multicentric origin, irradiation is the proper treatment. In collaboration with F. E. Adair the editor (G. T. Pack) has provided a most complete account of subungual melanoma (see p. 418).

Out of the 369 malignant tumours of the hand and foot at the Memorial Hospital for Cancer and Allied Diseases 180 were epidermoid carcinoma, 171 being of the

hand and 112 of the foot. In the article on carcinoma M. L. Mason classifies carcinomas of the hands and feet into (i) those connected with trauma, irritation, or X-rays, chemical, solar, mechanical, (ii) arising in a previous skin tumour, congenital, such as naevi, or acquired, such as warts, and (iii) arising from normal skin. A. W. Oughterson and R. Tennant divide the angiomatous tumours as follows: (i) Angiomas and angioblastomas, haemangioblastomas, and lymphangioblastomas; (ii) angio-myo-neuromas or glomus tumours, previously described as painful subcutaneous tubercle (W. Wood, 1812) and peritheliomas, but only recently regarded as arising in communications between arteries and veins (glomus). They contain myelinated nerve fibres and occur on the extremities, a third being sub-ungual. The outstanding symptom is pain (iii) Kaposi's idiopathic haemorrhagic sarcoma which has been described as showing 3 morbid changes, (a) inflammatory, (b) granulomatous, and (c) neoplastic. In the article entitled 'Tumours of the synovia, tendons, and joint capsules', A. Brunschwig describes ganglion, fibroma, xanthoma or the giant-celled tumours of the tendons and sheaths; it is regarded as open to debate whether the last-named are true tumours or local manifestations of obscure disturbance of fat metabolism, in favour of the metabolic origin is the occasional association with xanthelasma and hypercholesterolaemia. Malignant disease of the tendons and sheaths is quite rare. Histologically there are 4 types, synoviomias with a ground-work of round and spindle cells and cords or tubules of cuboidal or low columnar epithelium like cells, so-called spindle-celled sarcoma, round-celled sarcoma, and malignant change in osteo-cartilaginous or synovial tumours, or primary chondro-sarcomas. The prognosis is in general poor, the tumours are radio-resistant, and excision or, if the tumour is growing rapidly, amputation is indicated. B. I. Toley and N. I. Hignbotham collected from the Memorial Hospital for Cancer and Allied Diseases and the Hospital for the Ruptured and the Cripples 1,211 bone tumours, among which there were 47 primary in the hand (20) and the foot (27), the entire literature contains 609 cases, one-third being subcalcaneal spurs. Several forms of sarcoma occur. Carcinomatous metastases occurred in 2 of the authors' own cases. Among a number of cases of malignant melanoma Grey Turner figured a tumour of a hand crippled by osteo-arthritis.

- Paek, G. T. (1939) *Tumors of the Hands and Feet*, St. Louis and London.
 Turner, G. G. (1939) *Trans. St. John's Hosp. dermat. Soc.*, **28**, 107.
 Wood, W. (1812) *Edin. med. surg. J.*, **8**, 283.

FROST-BITE AND TRENCH-FOOT

See also B. E. M. P., Vol. V, p. 440, and Cumulative Supplement Key No. 528.

Clinical Picture

Trophic Disturbances

Resembling trench-foot—J. Ducuing *et al.* describe trench-foot as a trophic disease due to cold, wetness, and a slight infection. They saw no cases of real trench-foot in Spain during the Civil War, but many cases in which dry severe cold, even of very short duration, had caused trophic disturbances. The main sign was oedema of the foot which made walking difficult. There was no pain, but a sensation of tingling. The dorsal arteries of the foot could not be felt. There were no signs of infection. The oedema disappeared after several days, but often lesions appeared after that time; these varied from small ulcers to complete dry gangrene. Inflammation was very rare. The main aetiological factor appeared to be the intense dry cold, combined with the physical and moral exhaustion resulting from severe fighting. From a pathological point of view, the cases did not represent the picture of simple freezing. The main findings were arterial lesions, especially of the tunica intima. Prophylactically, warm socks, and shoes that do not exercise pressure should be worn. The skin should be kept treated with lanolin. The duration of time of standing on guard should be shortened so as to prevent extended immobility. Therapeutically tetanus antiserum should be injected. Very often no treatment is necessary even in severe cases as there occurs spontaneous restitution to the normal

state. The authors do not advise massage with snow, which only does more damage to the arterial functions. Local heat is recommended. The skin should be dehydrated with an alcoholic iodine solution. If the lesions are manifestly irreversible, surgical intervention is necessary.

Ducung, J., D'Harcourt, J., Folch, A., and Bofill, J. (1940) *J. Chu, Paris*, **55**, 385.

FUNGOUS DISEASES

See also B.I.M.P., Vol. V, p. 448, Cumulative Supplement, Key Nos. 529-544, and Surveys and Abstracts 1939, pp. 64 and 342.

Tinea Capitis

Treatment

Gentian violet. W. I. Spiller *et al.* employed a local application consisting of a 2 per cent solution of gentian violet and a 10 per cent solution of salicylic acid in 95 per cent alcohol, in cases of tinea capitis. The affected head was first shaved, then each day for 10 days it was cleared of crusts with soap and water, and then alcohol, and painted with the solution. The best results were obtained in patients infected with microsporon of the animal type, those due to microsporon of the human type or to trichophyton did not respond well.

Spiller, W. I., Sharp, W. B., and John, M. B. (1940) *Arch. Derm. Syph.*, N.Y., **41**, 370.

Other Fungous Infections

Treatment

Gentian violet and brilliant green. P. A. Maplestone and N. C. Dey report on the use of dyes in certain fungous infections. The authors trace the use of gentian violet in dermatology since its early mention by Hyde and Montgomery in 1900. In 1929 Acton and McGuire described a condition of purulent folliculitis common in India and the East ('coolie itch'), due primarily to a ringworm fungus with a secondary staphylococcal infection; the disease could be cured by applications of 5 per cent gentian violet solution. Since that time gentian violet has been in regular use in the dermatology department of the Calcutta School of Tropical Medicine for the treatment of this infection as well as for ringworm of the foot and allied conditions commonly known as 'mango toe'. Because this trichophyton infection is practically always complicated by a staphylococcal folliculitis it was felt that a combination of 2 dyes, 1 of which was particularly fungicidal and the other bactericidal, might prove a better remedy than gentian violet alone. In experiments on the effect of various dyes and chemicals on 4 species of fungi including *T. violaceum* (Maplestone and Dey, 1938) it was found that brilliant green was a very good fungicide but not so powerful a bactericide as was crystal (or gentian) violet. A combination of these 2 dyes resulted in a greatly enhanced fungicidal effect and a bactericidal effect equal to that of crystal violet alone. The authors used 10 per cent alcohol as the solvent as they found this never caused irritation. The lotion first used contained 2 per cent each of gentian violet and brilliant green in 10 per cent alcohol, a certain number of patients complained of irritation so the dyes were reduced to 1 per cent each.

The patient is instructed to pull out as many hairs as possible with forceps and the part is carefully swabbed with dry cotton-wool. A solution consisting of 1 per cent each of gentian violet and brilliant green is dabbed on twice daily; the patients improve quickly.

The same solution has been used for the treatment of interdigital infections of the hands and feet. These may be due to (i) *Epidermophyton floccosum* (cruris), (ii) *Actinomyces keratolytica* as mentioned by Acton and McGuire (1931), (iii) yeast-like organisms (monilia, saccharomyces) commonly seen on the palms but also described on the foot.

Paronychia (either due to *Actinomyces keratolytica* or a yeast-like organism) has also been successfully treated by the two dyes. The affected part is painted twice daily with a fine-pointed cotton-wool swab so that the solution may reach the space

between the nail and the paronychia tissue, cure generally results in about 1 month.

A. Dosa reported the use of a new ointment in the treatment of trichophytosis superficialis capitis, microsporon infections, and favus. He found that when Sabouraud's medium was supplemented by borax, the fungi disappeared in 24 hours, in a clinical test, the author found that 10 per cent borax added to Sabouraud's ointment cured trichophytosis and fungous disease in 3 or 4 days, after this period the hair was shampooed and, if necessary, a second course was given which ultimately cleared up the most obstinate cases. No irritation resulted from this treatment.

Acton, H. W., and McGuire, C. (1929) *Indian med. Gaz.*, **64**, 241

— — (1931) *ibid.*, **66**, 65

Dosa, A. (1939) *Derm. Z.*, **80**, 327

Hyde, J. N., and Montgomery, F. H. (1900) *A Practical Treatise on the Diseases of the Skin*, Philadelphia.

Maplestone, P. A., and Dey, N. C. (1938) *Indian J. med. Res.*, **25**, 603
(1939) *Indian med. Gaz.*, **74**, 391

GALL-BLADDER AND BILIARY DUCTS

See also B. F. M. P., Vol. V, p. 477, Cumulative Supplement, Key Nos. 545-550, Surveys and Abstracts 1939, pp. 48 and 344, and p. 13 of this volume.

Congenital Absence of Gall-Bladder

Associated with Carcinoma of Common Duct

H. I. Robertson *et al.* stated that congenital anomalies of the liver and gall-bladder, though rare, are sufficiently important to be considered in the differential diagnosis of liver disease. A survey of the literature revealed 96 cases of congenital absence of the gall-bladder, and this condition was often associated with stenosis and absence of the hepatic and common ducts. Such anomalies are by no means incompatible with life, and normal liver-function may be maintained. The authors reported a case of congenital absence of the gall-bladder associated with primary carcinoma of the common duct in a man of 45. No definite grouping of symptoms can be formulated to facilitate diagnosis of these conditions.

Robertson, H. I., Robertson, W. I., and Bower, J. O. (1940) *J. Amer. med. Ass.*, **114**, 1514

Double Gall-Bladder

I. Stolkind reported a case of double gall-bladder, found at necropsy in a man of 53. The gall-bladder, which was completely healthy and free from stones, was divided into 2 equal loculi by a septum containing a narrow orifice 2 cm. in circumference, uniting the 2 healthy cavities. The septum was definitely of congenital origin, due to a developmental defect. The author reviewed 39 reported cases, most of which were diagnosed only at operation, or necropsy. Operation has generally been performed because of cholecystitis or cholelithiasis. There are no signs or symptoms typical of this congenital abnormality.

Stolkind, I. (1940) *Brit. J. Surg.*, **27**, 760

Tuberculosis of the Biliary Tract

I. Ajello described cases of tuberculosis of the biliary passages and the gall-bladder which he had seen recently in small children. Normally the gall-bladder and biliary tract are immune from tuberculous infection. In the author's cases, both chronic cholecystitis and pericholecystitis was the clinical picture seen, and acute cholecystitis, though this was much rarer. The disease spreads haematogenously by the arteries or veins, or by the lymphatics from the ileocaecal region or by permeation of the biliary tract. In the author's opinion this form of tuberculosis is a sign of a local hypersensitivity or coexistent disease of the gall-bladder predisposing to tuberculous infection. The importance of allergy was stressed.

Ajello, I. (1940) *Riv. Pat. Clin. Tuberc.*, **14**, 1.

Gall-Stones

Clinical Picture

K. R. Trueman reviewed the symptomatology of common bile-duct stone in 219 cases; of these 61 per cent were women. Most patients were in the fifth, sixth, or seventh decades, the sixth being the commonest. The men in the series averaged 5 years older than the women. Pain was the commonest and most severe symptom (77.2 per cent of cases). In 63.9 per cent it was colicky in nature, usually intermittent. Less severe pain or merely abdominal distress was present in 13.7 per cent. In 22.3 per cent there was no history of any pain, 35.2 per cent had no history of jaundice at any time. Sepsis, as evidenced by chills and fever, had occurred in 34.2 per cent, usually associated with the attacks of colic and jaundice. The importance of these findings lies in the fact that stones were discovered in a large number of cases in which one or more of the characteristic triad of symptoms (colic, jaundice, and fever) were absent.

Diagnosis

Calcium bilirubinate pigment and cholesterol in faeces. I. Boerner *et al.*, in an examination of 2,003 stools, found in 67 of them the presence of calcium bilirubinate, cholesterol crystals, or both. In many of the cases the stools came from patients who were in hospital for investigation of some condition unrelated to the biliary tract. In 34 cases in which calcium bilirubinate alone was found in the faeces, excluding unstudied or doubtful cases, cholelithiasis was confirmed in 18 (72 per cent) of the remaining 25 cases. Of 14 cases in which cholesterol crystals alone were found in the faeces, there was only 1 case in which the diagnosis of cholelithiasis was confirmed. Of 3 cases in which both crystals and pigment were found, 1 case was not studied for cholelithiasis, and in the other 2 the findings were doubtful. The authors thought that the presence of calcium bilirubinate in the faeces should suggest further study of the patient to rule out cholelithiasis.

Calcium Carbonate Deposits in the Gall-Bladder

A. I. Cameron *et al.* record 2 unusual cases of extensive collection of calcium carbonate in the cavity of the gall-bladder. The gall-bladders were removed surgically. In the first case the cystic duct was blocked by a small dark faceted calculus, and the histological diagnosis was cholecystitis glandularis proliferans. The gall-bladder was occupied by a solid mass of sticky yellowish material (calcium carbonate 79.3 per cent) in which were embedded 91 small calculi (cholesterol 56, calcium carbonate 37 per cent). In the other case there was a cholesterol calculus impacted in the neck of the gall-bladder. The cavity of the gall-bladder was occupied by soft, yellow, homogeneous, putty-like material (64 per cent calcium carbonate). The occurrence of calcium deposit in the gall-bladder and in calculi is considered, and previous cases are recalled, among them Cameron and White's analysis of a gall-stone showing 86 per cent of calcium palmitate. A list of 28 cases of calcium carbonate deposits recorded since 1922 is divided into 5 groups: (i) milk of lime bile, (ii) milk of lime bile with calcium carbonate calculi, (iii) bile or bile-stained fluid with calcium carbonate masses, (iv) a plastic mass of calcium carbonate filling the gall-bladder, and (v) a harder mass of calcium carbonate filling the gall-bladder and incorporating other stones (case 1).

Boerner, I., Johnson, T. A., and Gianniny, M. (1939) *Amer. J. digest Dis.*, **6**, 466.

Cameron, A. I., and White, F. D. (1937) *Amer. J. med. Sci.*, **194**, 783.

- and Miltzer, S. (1938) *Canad. med. Ass. J.*, **39**, 441.

Trueman, K. R. (1940) *Proc. Mayo Clin.*, **15**, 283.

Cholecystitis

Treatment

Electro-surgical obliteration. H. Bailey and R. J. McNeill Love reported the results of 129 consecutive cases of Thorek's operation of the gall-bladder. The operation differs from cholecystectomy in leaving the portion of gall-bladder attached to the liver and destroying its function with the electrocautery. This obviates the necessity for drainage of the peritoneal cavity, and leaves no bare

area on the liver. There were no deaths in this series and 122 of the cases healed by first intention. Complications in the other 7 included wound infection, possibly due to contamination with bile at the time of operation. This operation results in a shorter convalescence than cholecystectomy, frequent dressings are avoided, and post-operative pain is far less.

Bailey, H., and Love, R. J. McNeill (1939) *Brit. med. J.*, **2**, 682

Cholangitis

Benign Stricture of Common and Hepatic Ducts

W. Walters and I. B. Lewis analyse 80 cases of benign stricture of the common and hepatic bile-duct operated upon by the first-named during 15 years. In 77 of the 80 cases previous operations on the biliary tract had been performed, in the 3 remaining cases the causes of obstruction were a neurofibroma at the junction of the common and hepatic bile-ducts, a calcified pancreatic cyst compressing the common bile-duct, and an inflammatory stricture. In 78 per cent of the patients cholecystectomy alone had been performed, in an additional 11 per cent both cholecystectomy and choledochostomy, and in 5 cases cholecystostomy alone had preceded the formation of a benign stricture. Symptoms of stricture appeared within 3 months of such operations in 52 cases, in 42 within the first week. The hospital mortality of the 80 cases operated upon for stricture was 12.5 per cent, and 19 patients died in their homes, in most instances from hepatic insufficiency or haemorrhage. 58 per cent of patients submitted to excision of the stricture or plastic operations on the common duct, and 68 per cent of those undergoing hepatico-duodenostomy or choledochoduodenostomy have remained well. In the most severe group of cases, in which no extrahepatic bile-duct remains above the stricture, surprisingly good results have in a few instances followed the establishment of an external biliary fistula and later implantation of the fistula into the stomach or duodenum.

Walters, W., and Lewis, I. B. (1939) *Proc. Mayo Clin.* **14**, 673

Adhesions of Cholecysto-Hepatic Flexure

J. R. Verbruycke discusses a syndrome caused by mechanical pull of localized adhesions between the hepatic flexure of the colon and the gall-bladder. The symptoms consist of the usual non-colic gall-bladder dyspepsia, or there may be less typical symptoms, there is dull pain in the epigastrium or the right upper quadrant of the abdomen, and in addition to gaseous distension there may be nausea. Nocturnal dyspepsia is not as great as is usual in cholecystitis, and a characteristic feature is that symptoms are mainly present during the day because of the upright posture with the consequent pull. If radiographically localized gas in the colon remains close to the same part of the gall-bladder in each of several films, the diagnosis should be reasonably certain. A better test for adhesions of the cholecysto-hepatic flexure is simultaneous examinations with barium and dye, a barium sulphate meal is given 24 hours before the first film, to fill the colon from above. Thirteen hours before the first film a gall-bladder dye is given. If the first film shows an angulated colon in absolute proximity to a small area on the fundus of the gall-bladder a second film is taken 3 hours later. If the relation of the 2 organs is exactly the same, a fat meal is given and another film taken 2 hours later. If the colon follows the contracting gall-bladder and the two shadows are as close as ever, the diagnosis is almost absolutely accurate. Cholecystectomy is followed by as perfect results as in other diseases of the gall-bladder.

Verbruycke, J. R., Jnr. (1940) *J. Amer. med. Ass.*, **114**, 314

Cholecystotomy in Old Age

J. H. Grindlay reports a case of successful cholecystotomy for complicated chronic cholecystitis in a woman, aged 86. The presence of gall-bladder disease and a stone had been shown radiologically 9 years previously, but on account of her age operation was not advised. Five years later she had coronary thrombosis with auricular fibrillation for a time. When 86 years of age she was again admitted to the Mayo Clinic for severe pain in the right upper quadrant of the abdomen, cardiac

enlargement and a loud apical systolic murmur, pyuria, and radiologically calcification in the region of the gall-bladder, and diverticulosis of the colon. Under regional anaesthesia, reinforced by small amounts of nitrous oxide, ethylene and oxygen, several gall-stones were removed from a much thickened gall-bladder which was drained. In addition, subacute perforating duodenal ulcer was found. For 2 days after the operation the temperature was 100° F., but otherwise her subsequent uneventful course was remarkable only for her cheerful co-operation: she was discharged from the Clinic with instructions to follow a modified ulcer diet, and since has been entirely free from pain.

Grindlay, J. H. (1940) *Proc. Mayo Clin.*, **15**, 121.

Cholecystocholedochostomy

B. O. C. Pribram writes on the operation of anastomosis of the gall-bladder with the common duct, or cholecystocholedochostomy, which corrects any obstruction in the cystic duct and is very satisfactory in simple biliary stasis. The indications for the operation include gall-stones, in which condition it maintains a functioning gall-bladder. In 32 cases there was only 1 death, but the period since operation is too small to judge ultimate results. The results, however, have been good in that the patient's appetite returns much sooner than after cholecystectomy, and it is not necessary to place the patient on a restricted diet.

Pribram, B. O. C. (1940) *Lancet*, **1**, 68.

GAS GANGRENE

Aetiology

Introduction of Spores by Injections

R. Regamey notes that gas gangrene after injection of drugs is not exceptional. It develops most unexpectedly after sterile injection. The aetiological agent is *B. perfringens* which has highly heat-resistant spores which will survive a temperature of 130° C. for 15 minutes. Every injection into the tissues is accompanied by a local reaction. Touraine found that post-injection gas gangrene followed injections containing adrenaline in 33 per cent of cases, in 22 per cent followed those containing caffeine, and the rest followed other injections. The local reaction therefore seems to form a focus minoris resistentiae on a mechanical and vasomotor base.

The bacillus originates, in the author's opinion, from an exogenous source, whereas some support the view of an auto-infection, *B. perfringens* being normally a harmless inhabitant of the digestive apparatus. The author thinks it far more probable that the *B. perfringens* enters the injection wound: (a) from the skin which cannot be sterilized, (b) from the solutions used for injection if not taken from sterile ampoules, (c) from the instruments if not boiled long enough, and (d) from the alcohol which is rarely sterile. Syringes should not be left in alcohol at all.

The author has experimented with the sterilizing power of alcohol and found that it is a violent protoplasmic poison for all non-sporulating bacteria. For sporing anaerobes, however, its antiseptic power is extremely weak. Spores can live in 90 per cent alcohol for nearly 3 months. He recommends application of iodine to the skin, and sterilization in an autoclave and testing of solutions which are not in sterile ampoules.

Regamey, R. (1939) *Schweiz. med. Wschr.*, **69**, 874.

Touraine, A. (1936) *Pr. med.*, **44**, 674.

Diagnosis

Radiography

J. F. Brailsford states that radiography can detect gas gangrene in a few minutes and without injury to the patient, before the formation of gas in the tissues has produced any clinical signs. Kelly *et al.* consider that X-irradiation gives the best therapeutic results. The X-ray appearances of gas gangrene depend on the nature of the anaerobic bacterial invasion and the stage of the disease. In penetrating

wounds the formation of gas bubbles round the foreign body will be the first indication of anaerobic infection. Such localized collections of gas are most often discovered during the X-ray examination of a wound a week or two after its production, and are usually associated with *B. sporogenes* or *B. perfringens*. Invasion of damaged tissues by *C. welchii* results in an acute fulminating gas gangrene. Often by the time the nature of the infection is suspected the invasion has passed beyond the bounds of the subcutaneous tissues, and X-rays will reveal separation of the muscle fibres by the interspersed linear collections of gas. X-rays may also be employed in treatment, and may obviate amputation. Kelly and his colleagues, with an experience of 140 cases, vigorously condemn amputation; they advise radiological treatment 3 or at most 5 days, 2 irradiations being given daily. The dosage is 100 r per port, filtered through 1 mm of aluminium.

Brailsford, J. I. (1940) *Brit. med. J.*, **1**, 247.

Kelly, J. F., Dowell, D. A., Russum, B. C., and Cohen, I. I. (1938) *Radiology*, **31**, 608.

Treatment

H. A. Britain reports a case of gas-gangrene associated with a compound fracture of the right tibia and fibula. The leg was reduced manually, débridement of the wound was carried out, and the leg was set in a bivalve plaster with a window over the wound. The patient was given a prophylactic dose of 12,000 units of gas-gangrene antiserum and 1,000 units of tetanus antiserum. The wound was examined every 2 hours. After 24 hours gas appeared at the lower aspect, and the patient's temperature was 99.5° F. Examination of the wound showed discoloration of several muscles which were completely excised and the wound placed on a Thomas splint. The wound was irrigated hourly with hydrogen peroxide alternating with acetic acid. A fan was arranged to provide a constant current of air and 16,000 units of gas-gangrene antiserum were given twice a day. Twelve hours later the patient's general condition had improved, and 4 days later there was no sign of gas gangrene. The wound was then cleaned and the plaster reapplied. The leg was then healing well. Stress is laid on the importance of constant examination of a wound when the fracture is in plaster, because if gas gangrene is not detected until the patient's condition is poor, it is almost certainly too late to save the limb.

Sulphonamide Drugs

D. Stephenson and H. I. Ross investigated the effect of the sulphonamides in experimental *C. welchii* and *C. septicus* infections in mice. It was found that sulphanilamide and sulphapyridine protected mice against a small number of lethal doses of *C. welchii* Type A injected intraperitoneally as a suspension of vegetative organisms in sterile soil suspension. Treatment with antitoxic serum was also effective in the case of a strain of high toxigenicity, but failed against a strain of low toxigenicity but probably of higher invasiveness. When the infected soil suspensions were injected intramuscularly considerably more organisms were necessary to produce a fatal result, and the drugs were of value only against a sublethal infection. Serum treatment was more effective, and protected mice even against lethal doses. With regard to *C. septicus* infections, sulphanilamide had little influence on infections of mice injected intraperitoneally or intramuscularly with suspensions of sporing and non-sporing organisms in calcium chloride solutions or sterile soil suspension. Sulphapyridine was more effective and, in large doses, saved 50 per cent of the animals. A single dose of antitoxic serum was at least as effective as sulphapyridine, but the best results were obtained when sulphapyridine was combined with serum, large doses of the drug being given immediately after infection, and serum up to 24 hours later. Neither sulphanilamide nor sulphapyridine had any influence on the course of infection with 2 strains of *C. oedematis*.

Gas-gangrene Antiserum

H. Vincent reviews the position of the specific treatment of gas gangrene and his own work and conclusions during and since the last war when it was so prevalent. The question of an efficient immunizing multivalent vaccine was decided against because, whatever technique (and he tried more than 30) was employed to sterilize the spores, the only satisfactory method was by the autoclave which also destroyed

the antigenic power of the vaccine. The value of early and adequate (60 c.cm.) intravenous injections of a multivalent gas-gangrene antiserum is shown. The serum should be active against at least 5 anaerobic micro-organisms, and the addition of the *Bacillus bellonensis* of Sacquépée and bacillus of Sordelli may be advisable; it should be both antimicrobial and antitoxic. Monovalent serums of different kinds mixed are not so efficient as the multivalent serums of horses each providing the multivalent serum, this plan Vincent has adopted. This serum has been most effective in extremely grave cases and acted very rapidly, the areas of gaseous infiltration returning to normal. A percentage of 90 recoveries in cases thus treated is contrasted with a percentage of 67.5 mortality in untreated cases in the last war.

Extensive Cauterization

I da C. Afonso advocates extensive cauterization instead of excision in gas gangrene. Cauterization checks the spread of the gangrene, and eliminates the gangrenous tissues; it also stimulates the neighbouring healthy tissues, besides transforming the necrotic tissues into a mass of products of combustion in which the development of anaerobic micro-organisms is impossible. The following treatment of large gangrenous areas is recommended. Careful delimitation of the necrotic zone; thorough washing of cavities, removal of foreign bodies and blood clot, and excision of muscle debris, cauterization of the neighbouring healthy tissues with a sharp-pointed cautery, encircling the gangrenous area with a line of superficial ignipunctures 1 cm. apart, and 3 cm. outside the necrotic area, incision of the necrotic tissues in several places, followed by insertion of the cautery in each incision, the cautery being moved about in every direction, so that no necrotic tissue is missed, and the intravenous injection of gas-gangrene antiserum, 1 or 2 injections being given of 80 to 100 c.cm. of serum in 1,000 c.cm. of physiological saline. Two days after cauterization most of the necrotic tissue should be dried and shrivelled, and can be readily removed with scissors.

Afonso, I. da C. (1940) *Lancet*, **1**, 644

Brittain, H. A. (1939) *Lancet*, **2**, 981

Stephenson, D., and Ross, H. F. (1940) *Brit. med. J.*, **1**, 471

Vincent, H. (1939) *Bull. Acad. méd. Paris*, **122**, 681

GASSING AND POISON GASES IN WAR

See also B. L. M. P., Vol. V, p. 502, and Cumulative Supplement, Key Nos. 552-557.

A. T. Jones, from his experience of treating 259 cases of gassing arising in industry, classified cases as mild when there was flushing of the face, slightly increased respiration and a painful cough, moderate when there was considerable respiratory embarrassment with distended cervical veins and some cyanosis, and severe. Treatment is directed to the relief of the immediate symptoms, principally in cases of chlorine gassing, and the prevention of serious after-effects, particularly in cases of phosgene gassing. For the relief of symptoms of gassing from chlorine and phosgene sodium thiosulphate solution, 10 per cent, may be atomized and inhaled. When there is pulmonary congestion, a carbon-dioxide-oxygen mixture should be inhaled. Oxygen alone is useful when oedema of the lung occurs.

Jones, A. T. (1940) *J. industr. Hyg.*, **22**, 235

Lung-irritant (Asphyxiant) Gases

Phosgene

E. Gillert emphasizes that the radius of the zone of effective concentrations of war gases is an important consideration in the selection of suitable locations for hospitals and first-aid stations in war. The extent of effective concentration depends upon such factors as the chemico-physical properties of the war gas, the type of munition used, and the configuration of the country. Under average conditions fatalities from phosgene were recorded up to 15 kilometres, phosgene poisoning over 20 kilometres, and the smell of phosgene up to 30 kilometres behind the front lines. High concentrations of gases may occur under special weather conditions, as in the

phosgene disaster in Hamburg (1928) and the case of a poison-laden fog in Belgium (1930). According to some authors 5 bombers, releasing 4,500 kilos of diphosgene, may make a district dangerous within a radius of 5 kilometres. The author approves of the Anglo-American order of 1918 according to which soldiers had to sleep with gas masks if within 7 kilometres of the front lines.

Gillert, I. (1939) *Med. Klink.*, **35**, 1071

Vesicant Gases

Mustard Gas

Effects on eyes - P. C. Livingstone and H. M. Walker studied the damage caused to the eyes of mature rabbits by single drops of liquid mustard gas. It was found that, in a small percentage of animals, there is some degree of natural resistance which definitely offers a barrier to the effects of the gas. In most cases, however, the immediate reaction is so intense and rapid that no local treatment can be hoped for which will prove helpful at this stage. The interaction of mustard and the secretions of the eye causes an alteration which leaves the mustard inactive as such after 15 minutes. Irrigations with lotions having a specific destructive effect upon the mustard is not recommended. A 2 per cent solution of sodium bicarbonate appears to be as helpful as any lotion. The use of atropine against the irritation of the iris leading to its contraction is important. Antiseptic washes, such as merthiolate 1 in 10,000, are of value. Oil drops, especially cod-liver oil, following irrigation have a favourable effect. Saturation of the system with ascorbic acid, given intravenously to 4 rabbits, had a remarkable effect in preventing the spread of keratitis.

J. Foster described the ophthalmic injuries resulting from mustard gas. The burn was divided into 3 stages by Bonnefor (1939), namely the period of impregnation, the established burn, and the period of decrescence. The first stage is very difficult to deal with as the gas is more readily absorbed by the cornea than the skin and the eye will only tolerate reagents active enough to deal with it in low concentrations. The action of the gas may be inhibited by applying greasy substances to the cornea. Addition compounds of the gas may be formed in the eye by using such substances as monochloramine-I or it may be oxidized to a less irritant substance with I in 10,000 potassium permanganate. Tusol and milton, substances liberating chlorine, may be used in the same way. Sodium bicarbonate has been used in the hope of hydrolysing the gas, but any effect it has is probably due only to irrigation. Hyper-tonic solutions have been advocated on the ground that they produce a freer flow of lymph in the conjunctiva, but their effect is probably only mechanical too.

Bonnefor, G. (1939) *Gaz. hebdom. Sci. méd.*, **60**, 168

Loster, J. (1939) *Brit. med. J.*, **2**, 1181

Livingstone, P. C., and Walker, H. M. (1940) *Brit. J. Ophthalmol.*, **24**, 67

GASTRITIS

See also B.E.M.P., Vol. V, p. 533

Differential Diagnosis

From Carcinoma

R. Schindler reported 7 cases in which great difficulty was experienced at X-ray examination or at gastroscopy, or during surgical operation, in making a diagnosis between gastric tumour and gastritis. In these cases microscopical examination showed unusually severe gastritis of different types, sometimes typical hypertrophic gastritis, but also atrophic gastritis with compensatory hyperplasia or lymphocytic infiltration. In such cases the question arises as to what should be done. If there is pyloric obstruction or if there is an isolated polypoid gastritis of the antrum, immediate resection is indicated. In most cases thorough resection should be delayed until proper microscopical examination has proved the presence of carcinoma. The frequency of gastritis simulating tumour formation should not be underestimated.

Schindler, R. (1939) *Amer. J. Digest. Dis.*, **6**, 523

Chronic Atrophic Gastritis*Treatment*

Desiccated hog's-stomach - L. Schiff and S. Goodman treated 5 patients with a gastroscopic diagnosis of chronic atrophic gastritis, not associated with other gastric disease, pernicious anaemia, protein or obvious vitamin deficiency, with ventriculin (hog's-stomach extract), in a daily dosage of 30 g. to 60 g. All the patients showed marked symptomatic improvement together with disappearance of the atrophic changes. In 2 of the patients withdrawal of ventriculin was followed by the reappearance of the atrophic changes as observed through the gastroscope, and in one patient the previous symptoms also returned. The authors suggested that desiccated hog's-stomach may make up for the absence of a substance present in the normal stomach.

Schiff, L., and Goodman, S. (1940) *Amer. J. digest. Dis.*, **7**, 14.

GERMAN MEASLES

See also B.I.M.P., Vol. V, p. 547, and Cumulative Supplement, Key No. 559.

Complications*Rheumatic Manifestations*

R. A. Bennett and W. S. C. Copeman contribute notes of unusual features in the course of an epidemic of German measles (rubella) among the British Expeditionary Force in France during 1940, when more than 300 cases came under their observation. In 4 cases the onset was very severe, and in 2 of these 4 cases for a time suggested meningitis. Early in the epidemic the cases were usually exceptionally mild, but became severe towards the end of the epidemic. Much stress is laid on the various 'rheumatic' manifestations ranging from transient muscular pains lasting 1 or 2 days in 15 per cent of the cases to those of rheumatic fever. In some patients the muscular pains occurred in positions where fibrositis had previously been troublesome. In 10 per cent of the patients there was a secondary rise of temperature after an afebrile period of 2 or more days. In many patients there was from the second day of the disease pain in the joints, which lasted for 2 days. Enlargement of the lymphatic glands was widely spread, and not confined to the posterior cervical region and, not going down with the appearance of the rash, but lasting 10 days, suggested glandular fever. Leucocyte counts generally showed leucopenia with a relative lymphocytosis. Desquamation after fading of the rash was profuse in many cases. In 8 per cent of the cases there was a relapse.

Bennett, R. A., and Copeman, W. S. C. (1940) *Brit. med. J.*, **1**, 924.

GLANDULAR FEVER

See also B.I.M.P., Vol. V, p. 559, and Surveys and Abstracts 1939, p. 348.

Clinical Picture*The Exanthem*

H. J. Templeton and R. T. Sutherland describe the exanthem which sometimes occurs in acute mononucleosis and report 17 cases of skin eruption among 99 proved cases of the disease. The rash often almost identical with that of German measles, is morbilliform in character. A macular eruption occurs in the febrile type. Skin rashes are rare in the glandular and angiose types of the disease. The trunk is usually involved and the face quite commonly. Itching is mild or absent. The rash appeared on the third to the twentieth day and lasted from 3 to 7 days. There was no desquamation.

Templeton, H. J., and Sutherland, R. T. (1939) *J. Amer. med. Ass.*, **113**, 1215.

Diagnosis

The Agglutination Reaction

R. Demanche states that the agglutination reaction is of high value in the diagnosis of glandular fever. There are forms of the disease without adenopathy or with local adenopathy only, and there are also visceral forms, 'typhoid' forms and 'scarlatinoid' forms. The common feature is the mononucleosis, which, however, is sometimes very slight and is late in appearing. A good many infectious diseases show also very few polynuclear cells and differential diagnosis is sometimes very difficult. The agglutination test for glandular fever is very specific. In diseases of the blood and infective conditions which closely resembled infective mononucleosis the test was negative, whereas in 147 cases of glandular fever it was negative in one only.

Demanche, R. (1939) *Pr. méd.*, **47**, 1614

Treatment

Sulphapyridine

H. S. Stannus and G. M. Findlay reported a case of glandular fever of the anginose type in a girl of 18 years. There was a prodromal period of 10 days consisting of headache, rising temperature, and constipation. This was followed by sore-throat, then swelling of the neck and oedema of the fauces. The spleen became enlarged but there was no sign of lymph-gland enlargement. The blood picture was typical of the condition. The patient was given 2 intramuscular injections of sulphapyridine 0.5 g. and 1 g. in oily suspension, the following day 2 further injections, each of 1 g. were given. Next day a further injection of 1 g. was given. Following the first day's injections, the temperature fell from 104° F. to 98° F., next day it rose to 102° F., then fell the following day to 98° F., rising the same day to 100° F. Next day it fell to normal and remained so. The patient recovered. The disease was transmitted to a rhesus monkey by intramuscular injection of 4 c.cm. of whole blood of the patient.

Stannus, H. S., and Findlay, G. M. (1939) *Lancet*, **2**, 595

GLAUCOMA

See also B.I.M.P., Vol. V, p. 575, and Surveys and Abstracts 1939, pp. 129 and 349

Aetiology

Anxiety States

M. J. Schoenberg discussed the part played by anxiety states in the pathogenesis of primary glaucoma. In a case of bilateral glaucoma one eye was successfully operated on and the tension of the other was controlled by local medication. Whenever the patient became upset, as by quarrels or nervousness over business problems, the tension in the unoperated eye rose. This was shown by discomfort or pain, and by seeing of haloes. Another similar case, in which attacks were provoked by drunken bouts in the patient's husband, was reported. In all 11 cases were discussed. Schoenberg summarized the physiological effects of anxiety and stated that they affected the body in the same way as a sudden large increase of adrenaline in the blood stream. In the glaucomatous eye the pupil becomes dilated and the tension rises. Stress was laid on the fact that such rises of tension may be avoided by proper attention to the patient's emotional life.

Radiotherapy

L. Bothman reported a case of glaucoma following large doses of radium and X-ray therapy. The outstanding pathological change was the breaking up of the anterior uveal pigment epithelium and its dispersion over the anterior surface of the iris and in the spaces of Fontana, with little vascular change, and no synechiae.

Bothman, L. (1940) *Arch. Ophthalm.*, N.Y., **23**, 1198

Schoenberg, M. J. (1940) *Arch. Ophthalm.*, N.Y., **23**, 76.

GLYCOGEN DISEASE

See also B E M P, Vol V, p. 586, and Surveys and Abstracts 1939, p. 351.

Aetiology

In an investigation into post-mortem hepatic and muscular glycogenolysis in hyperinsulinism and glycogen disease, H. P. G. Seeckel found that in 2 adult cases of spontaneous hypoglycaemia—1 probably due to pancreaticogenic hyperinsulinism due to carcinoma of Langerhans' islands with hepatic metastases, the other of neurogenic hyperinsulinism, with a fibroma above the liver—there was a comparatively high hepatic and muscular glycogen content and an approximately normal or only slightly decreased post-mortem hepatic glycogenolysis. As in glycogen disease there is almost complete inhibition of post-mortem glycogenolysis, it is argued that typical glycogen disease cannot be caused by either of these forms of hyperinsulinism.

Seeckel, H. P. G. (1939) *U. clin. Invest.*, **18**, 723.

Pathology and Morbid Anatomy

F. R. B. Atkinson reviewed the history and reported cases of von Gierke's disease, or glycogen disease, first described in 1929. So far 59 cases had been reported in the literature. In addition a number of doubtful cases had been reported. The disease occurs in early childhood and is occasionally familial, brothers and sisters being affected. It has been suggested that the disease is inherited as a Mendelian recessive character. Twenty-one necropsies are recorded in the literature. The liver is always enlarged owing to the presence of excessive glycogen and the spleen may also be enlarged. Glycogen is also found in the kidneys and sometimes in other organs such as the heart. A large abdomen due to the greatly enlarged liver, infantilism, and a greatly reduced resistance to infection are the outstanding symptoms and signs in the condition. A low blood-sugar, producing no symptoms of hypoglycaemia, and a high blood-glycogen level are constant findings. Von Gierke's disease must be differentiated from Niemann-Pick's and Gaucher's diseases. A biopsy of the liver establishes the diagnosis in doubtful cases. The disease is not necessarily fatal, and irradiation of the liver by X-rays has been used with some success in a few cases.

Atkinson, F. R. B. (1939) *Brit. J. Child. Dis.*, **36**, 261.

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also B E M P, Vol V, p. 599, Cumulative Supplement, Key Nos. 569-574, and Surveys and Abstracts 1939, p. 352.

Relation between Iodine and Affections of the Thyroid Gland

In an exhaustive monograph on the geographical distribution of iodine and the incidence of goitre, J. I. McClelland considers the question of the existence of 'Jodbasedow' or the supposed transformation by iodine medication of simple goitre into toxic adenoma, as was strongly advocated in 1910 by F. Kocher who forbade the use of iodine for sterilizing the skin in cases of goitre. The distinction between true Basedow's disease and *Jodbasedow* held in German-speaking Europe is regarded as the same as that between toxic goitre and toxic adenoma held in the United States, where it is claimed that toxic adenoma is benefited by overdosage of iodine. It is concluded that toxic adenoma is not caused by iodine treatment.

McClelland, J. I. (1939) *Iodine and the Incidence of Goiter*, University of Minnesota Press, p. 95.

Pathology of the Thyroid Gland

D. Marine reviews the physiology, the principal endocrine interrelations of the thyroid, and the relations of the vitamins to thyroid function. The thyroid of vertebrates in its normal or colloid stage morphologically suggests a storage gland, whereas in its hyperplastic stage it is an actively secreting gland, it rapidly—in a

few hours—passes from one stage to the other. The hyperplastic or hypertrophic stage is due to stimulation by the thyrotrophic hormone of the anterior pituitary, but not necessarily an increased production of the thyroid hormone; it is regarded by Marine as the initial stage of goitre. The colloid or resting stage represents the return to the normal or quiescent state from the hyperplastic phase. An atrophic stage represents the permanently exhausted condition of the thyroid. Although the thyroid has a rich supply of vasomotor nerves its stimulation is humoral, not through nervous channels. Thyroxine appears to be the active chemical fraction only of the true thyroid hormone, for it is less powerful than the iodine-equivalent amount of desiccated thyroid and the physiological activity of desiccated thyroid is proportional to the total iodine rather than the thyroxine. A substance identical chemically and physiologically with thyroxine has been obtained by the hydrolysis of iodized casein with weak alkali and heat (Ludwig and von Mutzenbecher). The thyroid has a unique selective action in fixing iodine reaching it by the blood. Bromine is also present in larger amount in the thyroid than in any other tissue—it does not produce involution of thyroid hyperplasia, but there is some clinical evidence that bromine combined with iodine may be more beneficial than iodine alone in the treatment of goitre. The interrelations of the thyroid with the other endocrine glands make it difficult to determine how far the old conception of a purely thyroid disease should be retained. The relations with the pituitary, the gonads, adrenals, parathyroids, and thymus are summarized, and the thymic enlargement in toxic goitre and acromegaly suggests some measure of antagonism between the thyroid and thymus, but thymectomy does not seem rational. In connexion with the relation between the vitamins and thyroid function it is pointed out that vitamin C appears to have more effect than vitamins A and B on the thyroid. Thyroxine reduces the content of ascorbic acid and glutathione in the blood, thus indicating that more of these active agents is consumed when oxidation processes are increased. As a whole, however, the evidence indicates that vitamins A, B, C, and D do not specially influence the thyroid and their administration does not appreciably influence either myxoedema or toxic goitre.

Ludwig, W., and von Mutzenbecher, P. (1936) *Hoppe-Seyl Z.*, **244**, p. iv.
Marine, D. (1939) *Bull. N. Y. Acad. Med.*, 2nd ser., **15**, 790.

Fatal Sporadic Congenital Goitre

L. Solis-Cohen and M. Steinbach record the case of an infant, weighing 7 lb. 10 oz. at birth, with 6 toes on both feet and 6 fingers on the right hand. Death from progressive dyspnoea occurred within 48 hours after birth. The large bilobed thyroid weighed 41 g., the normal thyroid weighing 1 to 2 g. at birth in non-goitrous regions, and in endemic goitrous areas 5 to 10 g. This, therefore, is of exceptional weight. Microscopically the acini were hyperplastic and devoid of colloid. The thymus showed simple hypertrophy and weighed 10 g. The mother's blood gave a positive Wassermann reaction, as did that of the umbilical cord, but the authors considered that this had not any bearing on the goitre.

Solis-Cohen, L., and Steinbach, M. (1939) *Amer. J. Dis. Child.*, **58**, 1067.

Treatment

Thyroid Intoxication

Heart-block.—M. Asner and J. F. Dorsey report a case of complete heart-block resulting from excessive dosage with thyroid extract. Disturbances of rhythm, including partial heart-block, are not infrequent in true hyperthyroidism, but complete auriculo-ventricular dissociation is rare, only 10 cases of complete heart-block having been reported. No case similar to the present, resulting from the administration of thyroid extract, has previously been reported.

A 33-year-old female was admitted complaining of diarrhoea of 7 days' duration and vomiting after food. Three years before admission the patient had been advised to take thyroid for obesity. There was no supervision of the dosage, the patient having resorted to the medication whenever she noticed an increase in weight. For the 5 weeks prior to the present illness she had taken the equivalent of from 12 to 15 gr. U.S.P. extract daily. The heart was not enlarged; the sounds were of good quality, regular and slow; rate 32. Parenteral glucose-saline and iodine

were given. An electrocardiogram showed an auricular rate of 94 and ventricular rate 26 to 33. During the next 36 hours the patient remained anuric but responded finally to several intravenous injections of hypertonic saline, signs of bronchopneumonia were elicited at the left base. The pulse rate was now 88 and the rhythm regular, a second electrocardiogram showed normal sinus rhythm, both auricular and ventricular rates being 88. Parenteral fluids containing saline, glucose, and sodium bicarbonate were continued until slight pitting oedema of the ankles appeared. The urinary output gradually increased, the signs at the left base cleared, the sallow appearance disappeared and the patient was markedly improved. The patient was discharged on the thirty-third day, the electrocardiogram being normal and the metabolic rate 18 per cent.

A brief discussion of the factors involved in the pathogenesis of complete heart-block in hyperthyroidism is given. There is little evidence that the block is due to anatomical lesions. There is evidence of deranged nutrition of the myocardium during experimental hyperthyroidism, the heart muscle is depleted of glucose, creatine, and phosphocreatine. It would seem not unlikely, then, that the transient, and in certain cases paroxysmal, nature of some of the cardiac arrhythmias observed during the course of hyperthyroidism is due to chemical changes, many of which are readily reversible.

ARNOLD, M., and DORSEY, J. F. (1939) *New Engl. J. Med.*, **221**, 336

Toxic Goitre

Causation of Exophthalmos

From experiments on guinea-pigs, normal and thyroidectomized, D. L. Paulson of the Mayo Clinic confirms the view of W. I. Benedict that oedema of the orbit is the fundamental cause of exophthalmos in toxic goitre. This, together with degeneration of extra-orbital, skeletal, and cardiac muscles, he induced by the administration of an anterior pituitary extract containing a potent thyrotrophic factor. The retrobulbar oedema was more prominent in the thyroidectomized animals whenever the muscle changes occurred in both normal and thyroidectomized animals. Clinically, exophthalmos does not correspond with the level of the basal metabolic rate, it may even occur in patients after operation for toxic goitre and with partial myxoedema, in progressive exophthalmos the eyelids are often oedematous (Haines).

New Clinical Test

Galactose test. T. I. Althausen *et al.* describe a new clinical test for estimation of the activity of the thyroid, based on the rate of intestinal absorption of galactose. This test consists in the oral administration of galactose followed by estimations of the galactose in the blood at intervals of 30 and 60 minutes later. The test was carried out on 130 hyperthyroid patients and 124 other subjects as controls. The average maximal concentration of galactose in the blood of hyperthyroid patients was 3 times greater than in the controls. Clinically, the test proved to be comparable in reliability to estimations of the basal metabolic rate. After thyroidectomy, the galactose test became normal in practically every case. Advantages of the test are that it is more sensitive than the basal metabolic rate in cases of low-grade hyperthyroidism; its outcome, also, is not influenced by hyper-ventilation in anxiety states or by cardiac dyspnoea. A disadvantage is that the presence of hepatic insufficiency, or of Paget's disease, interferes with its use for the diagnosis of thyroid disease. Abnormally low galactose tolerance curves were observed, indicating that the test could also be employed in the diagnosis of the latter condition.

Clinical Picture

Galactose tolerance test. N. I. MacLagan found that in 10 out of 12 cases of toxic goitre definite impairment of hepatic glycolytic function was present. These were clinically severe cases with basal metabolic rates ranging from +20 to +80 (average +55) per cent, and indicating liver damage in toxic goitre, although this change has not been generally recognized.

Exophthalmos in presence of sympathetic paralysis. W. Russell Brain records bilateral exophthalmos in toxic goitre in the presence of sympathetic paralysis due

to syringomyelia. The ocular sympathetic was completely paralysed on the right and partially on the left side. The patient developed exophthalmos, with slightly more retraction of the left than of the right upper lid. It was therefore concluded that the sympathetic does not play any part in the production of exophthalmos in this condition. After medical treatment the exophthalmos recovered, leaving the left palpebral fissure normal and the right upper lid slightly ptosed.

Treatment

Hippuric acid test as guide to management—S. F. Haines *et al.* investigated the capacity for excreting hippuric acid in 17 cases of adenomatous goitre with hyperthyroidism and in 61 cases of exophthalmic goitre. They found that in the majority of cases the excretion was reduced, the tendency being for this to take place if the basal metabolic rate were raised. There was, however, no correlation between the results of the test and other aspects of hyperthyroidism. The authors therefore concluded that the test is of little clinical significance, but is of interest because it shows that there must be some, if only temporary, upset in the physiology of the liver in hyperthyroidism.

Magnesium glutamate—I. F. Hueber, on the basis of previous demonstration by himself and Lehi that magnesium compounds have a regulating action on the heart in experimentally produced cardiac arrhythmias, investigated the effect of magnesium in disorders associated with increased metabolism such as hyperthyroidism. In 6 cases of this disease the basal metabolism was measured on the day of admission to hospital, then, after 5 to 7 days' rest in bed during which injections of distilled water were given, the basal metabolism was again determined. In those patients who still had a high basal metabolism, 3 daily injections of 10 c.cm. of a 10 to 20 per cent solution of magnesium glutamate were given. It was found that intramuscular injections gave rise to no irritation, whereas the intravenous route produced an unpleasant sensation of heat. After 3 days of treatment the patients experienced relief of symptoms, and tachycardia was lessened. The basal metabolism which ranged from 25 to 60 per cent above normal was reduced to 7 to 13 per cent above normal. The improvement was prolonged in most cases and, if the basal metabolism subsequently rose, it could be again reduced by another course of treatment.

Althausen, T. L., Lockhart, J. C., and Soley, M. H. (1940) *Amer. J. med. Sci.*, **43**, 342.

Benedict, W. L. (1938) *South. med. J.*, **31**, 321.

Brain, W. R. (1939) *Lancet*, **2**, 1217.

Haines, S. F. (1939) *Proc. Mayo Clin.*, **14**, 831.

— Magath, T. B., and Powers, M. H. (1939) *Proc. Mayo Clin.*, **14**, 495.

Hueber, I. F. (1939) *Wien. klin. Wsch.*, **52**, 932.

MacLagan, N. I. (1940) *Quart. J. Med.*, N.S., **9**, 157.

Paulson, D. I. (1939) *Proc. Mayo Clin.*, **14**, 828.

Tumours

Malignant Aberrant Thyroid

M. A. Hameed reports a case of a primary malignant cystadenoma in an aberrant lateral thyroid with metastases in the local lymph glands in a man, aged 25, in good general health who had noticed a swelling in the neck on the left side from the level of the hyoid bone to the third tracheal ring. It was removed and, when its malignant nature was recognized histologically, a further operation was carried out. The thyroid was somewhat enlarged and microscopically showed hyperplasia and adenomatous changes, but was regarded as not primarily malignant. From a summary of the embryology of the thyroid it is suggested that lateral aberrant thyroids are derived from cells of the posterior portion of the pharynx, which, in migration, have failed to fuse with the median thyroid, remain as foetal 'rests,' and may awake to tumour formation. The patient made an uneventful recovery and a year later was free from recurrence. The author was not aware of any record of this disease in India.

Hameed, M. A. (1940) *Brit. med. J.*, **1**, 344.

GONORRHOEA

See also B.L.M.P., Vol VI, p 1; Cumulative Supplement, Key Nos. 575-578; Surveys and Abstracts 1939, pp 155 and 356, and p 90 of this volume

Gonorrhoea in Males*Treatment*

Sulphapyridine - S. H. Johnson *et al.* used sulphapyridine in the treatment of gonococcal urethritis in the male. To 80 patients, between the ages of 17 and 48 years, 3 g. of sulphapyridine were given daily for 4 days, then 2 g. daily for 6 to 10 days in divided doses. In one hospitalized patient the treatment was continued for more than 14 days. Of the patients, 17 either failed to complete the course of treatment or to complete the tests for cure. Of the other patients the majority were followed for 2 or more months. Of the patients followed, 54 had acute urethritis and 42 were cured, 4 had subacute urethritis and all were cured, and 4 had chronic urethritis and 3 were cured. Urethral discharge persisted for an average of 2.77 days in the cured patients, a great advance over older forms of treatment. Complications occurred in this series, all in those in whom the treatment failed. There was 1 case of unilateral epididymitis, 1 of bilateral epididymitis, and 2 of arthritis.

Toxic reactions to the drug occurred in 45 patients and in 11 they were severe. In the severe cases, for example leucopenia, the drug was stopped. The average blood sulphapyridine level was about equal in the successes and failures, namely 2.8 mg. and 2.3 mg. per 100 c.c.m. In the failures, the reasons for the failures being discussed, 6 of the patients had not completed the treatment owing to severe reactions. The authors concluded that sulphapyridine is the most efficient of the sulphanilamide derivatives in the treatment of gonococcal urethritis in the male. Of 19 patients 68.4 per cent. previously resistant to other sulphonamide derivatives were cured with sulphapyridine.

Sulphapyridine and mercuric oxycyanide irrigations - N. S. Taylor reported results obtained with sulphapyridine in one series of 100, and another of 150 cases of acute gonococcal urethritis. His technique was as follows: on the patient's first attendance, if the urethral discharge had been present for less than 7 days, $\frac{1}{2}$ grain of eufllavine in the form of a pill was given 3 times daily, and complete lavage with mercuric oxycyanide irrigations was continued, for the second week potassium permanganate, 1 in 8,000, was substituted. All irrigations were given at a temperature of 105° F. If the infection had been present for more than 7 days at the time of the first attendance, sulphapyridine was begun at once, and given for 14 days in a dosage of 2 g. daily. At the end of the third week an oxycyanide lavage was given, after which prostatic massage was performed. If the resultant bead was negative for pus and gonococci, the patient was given complete lavage with silver nitrate, 1 in 10,000, for 3 days, followed by anterior irrigation for a further 3 days with 1 in 5,000 silver nitrate. After a week without treatment, during which he was advised to take alcohol in moderation, the gonococcal complement-fixation test was made and a 200 million dose of a gonococcal vaccine was given intradermally as a provocative. After a further 2 days the arm was examined for local reaction, and a bead resulting from massage of the left vesicle examined microscopically. Next day the right vesicle was similarly treated. The patient was considered cured if there was no urethral discharge following the silver nitrate irrigations or the alcohol, no discharge or local reaction following the vaccine, a negative complement-fixation test, and easy passage of sound, and absence of pus and gonococci from the vesicular beads. This method of treatment produced in the first series of 100 cases 96 per cent of cures, which included 64 per cent absolute cures and 32 per cent apparent or clinical cures (those who failed to return for some of the final tests, but whose urines were clear, and who had passed all tests until they defaulted). In the second series of 150 cases, the results were similar.

L. L. Prebble employed sulphapyridine in 240 cases of gonorrhoea in all stages of the disease. The routine treatment consisted of 3 g. daily for 1 week, followed by 1.5 g. daily for a second week. In almost all cases irrigations of 1 in 8,000 mercuric oxycyanide at a temperature of 105° F. were given. Of the 246 cases 41 defaulted too early to assess the value of the drug. Of the others there were 101 cures, 47 apparent cures, and 12 failures or relapses in acute cases, and 35 cures, 2 apparent

cures, and 8 failures or relapses in chronic cases. If apparent cures (cases in which the patients failed to complete the tests for cure) are considered as real cures, the percentage of cures in early acute cases was 92.5 per cent and in chronic cases 82.1 per cent.

Johnson, S. H., Leberman, P. R., Pepper, D. S., and Lynch, H. (1939) *Amer. J. med. Sci.* **198**, 594.

Prebble, F. E. (1940) *Brit. med. J.*, **1**, 89.

Taylor, N. S. (1940) *Brit. med. J.*, **1**, 88.

Gonorrhoea in Both Sexes

Treatment

Sulphanilamide. A Jacoby *et al.* treated 100 patients, shown by clinical and bacteriological tests to have gonorrhoea, with 80 grains (5.2 g.) of sulphanilamide every 24 hours for 4 days and 40 grains (2.6 g.) for the next 7 days. The fluid intake was restricted to 1,000 c.c.m. per day. No other treatment was given. Twenty-five per cent of the patients showed some toxic reaction, but 45 per cent of them were cured in an average of 13.7 days. Twenty-three patients were given sulphanilamide as in the first group and intravenous vitamin C every other day starting with 100 mg. and increasing each dose by 100 mg. until a 300 mg. dose was reached. Forty-eight per cent of these patients were cured in an average of 11.0 days. Forty-three other patients received sulphanilamide plus gonococcal vaccine to assist the formation of antibodies. Of these 81 per cent were cured in an average of 19.3 days. Jacoby *et al.* concluded that sulphanilamide is an effective drug in the treatment of gonorrhoea, especially if it is combined with some other factor to make its action easier or to produce antibodies.

Albucid.—R. Ullrich recommends albucid (*p*-aminobenzenesulphonacetamide) in the treatment of gonorrhoea because of its solubility, its rapid excretion, and low toxicity. An average dose in a course is 31.5 g. (3 tablets 3 times a day for 7 days), the course can be repeated if necessary after 6 to 12 days. Among 56 stationary cases he had 50 cures with an average duration of 30 days; 38 patients were cured after the first course and 12 after the second. In 61 ambulant male cases, 57 were cured, of 16 women, 11 were cured. Albucid treatment should be commenced immediately and combined with specific local treatment. Vaccine treatment should only be used if there are complications. By-effects after albucid were very few: albuminuria, paraesthesia, drowsiness, and nausea.

Artificial hyperpyrexia and sulphanilamide.—I. Belt and A. W. Folkenberg reported that, of a series of 100 patients suffering from gonorrhoea and treated by a single session of hyperpyrexia of 10 hours' duration, at a rectal temperature of 106.7 F., 87 were found, at an adequate follow-up, to be free from gonococci. Of these, 63 had had the disease for an average of 4 weeks before fever therapy, and were classified as acute; in this group there were 4 failures (84 per cent cures). Of the remaining 37 patients who had chronic gonorrhoea, 3 failed to be cured (92 per cent cures), the average duration of the disease in this group had been 5.4 years. Of the 13 patients not cured after a single session, 5 were given a second treatment of 10 or 12 hours, and were cured. The authors outlined a plan for combined fever therapy and chemotherapy. Patients were instructed to take 20 grains of sulphanilamide, 4 times a day for 2 days. A fever session of 5 hours was then given, and repeated every other day for 3 treatments. Sulphanilamide, 20 grains 4 times a day, was given on the alternate days. Of 49 patients thus treated, there were 7 failures (86 per cent cures).

Belt, I., and Folkenberg, A. W. (1940) *Arch. phys. Ther.*, **21**, 203.

Jacoby, A., Drummond, A. C., and Ollswang, A. H. (1939) *New Engl. J. Med.*, **221**, 102.

Ullrich, R. (1939) *Derm. Wschr.*, **109**, 967.

Vulvovaginitis in Children

Treatment

Diethylstilboestrol.—J. D. Russ and C. G. Collins employed diethylstilboestrol

orally in 25 cases of vulvovaginitis in children. Treatment varied from 7 to 18 days, irrespective of the age or weight of the child or of the duration of symptoms. 1 mg tablet of the drug was given crushed and placed in milk 3 times a day, until 20 had been given. In 22 cases negative smears for pus and gonococci were obtained after 7 days of treatment. Two cases required 9 and 18 days of treatment respectively. The authors concluded that, on account of the rapidity of cure, the absence of toxic effects, and the ease of administration diethylstilboestrol is an ideal drug for the treatment of vulvovaginitis in children.

Mandelic acid buffer and oestrogen—T. H. Cherry treated *Trichomonas vaginalis* infection by building up the general body resistance with iron tonics and vitamin therapy, and by attempting to produce an acid reaction of the vaginal secretion by insufflating the vagina, 3 times weekly, with a powder prepared as follows. A concentrated solution of sodium hydroxide and mandelic acid in molecular proportions was stirred until dissolved, then the water was evaporated. The residue was washed with ether to eliminate any remaining mandelic acid. The mass was then pulverized, and to this powder was added 4.29 g. sodium mandelate, 3.16 g. mandelic acid, and 1.00 g. glucose. The pH of this buffer is 3.0. After about 6 insufflations, all cases became free of the trichomonads, with a lowering of the pH from 3.5 to 4.5. When this occurred local treatment was discontinued and the patients were injected with 30,000 I.U. of oestrogenic hormone, 3 times weekly, for 3 weeks.

Silver picrate suppositories—J. W. Holmes *et al.* report on the treatment over a period of 3 to 29 weeks of children with gonococcal vulvovaginitis by silver picrate suppositories, each containing 1 grain of silver picrate. Most of the cases improved, the discharge and gonococci disappearing in from 1 to 2 weeks, the average for all cases being 3.2 weeks. Six of the cases recurred during six months' observation. It was concluded that the suppositories were a simple and quite successful method of treating vulvovaginitis.

Acidulation of vagina—R. W. Daftlinec stated that acidulation of the vagina appears to offer the best solution to the problem of treating gonococcal vulvovaginitis. This is satisfactorily effected by the use of acidulated sugar tablets, which, moreover, avoids the occurrence of endocrine side-effects with oestrogens. Treatment is also less expensive than that by endocrine preparations. As a result of a five-year study of the hospital treatment of the condition, the author found that local treatment with most of the known non-toxic antiseptics was ineffective, and that oestrogenic treatment gave unsatisfactory results. Gonococcus filtrate and sulphanilamide also were not very satisfactory. On the other hand acidulated sugar tablets gave immediately favourable results in all but 1 of 6 cases. With the use of 3 tablets a day, introduced into the vagina, a pH of 4.0 or 4.5 could generally be maintained.

Cherry, T. H. (1939) *Amer. J. Surg.* **46**, 358.

Daftlinec, R. W. (1940) *Arch. Pediat.* **57**, 295.

Holmes, J. W., Jones, J. A., and Gildersleeve, N. (1939) *J. Pediat.* **15**, 86.

Russ, J. D., and Collins, C. G. (1940) *J. Amer. med. Ass.* **114**, 2446.

Keratosi s Blenorrahgia

Actiology

F. Epstein discusses the pathogenesis of keratosi s blenorrahgia and presents a study of 72 cases from the literature and 3 new cases. Considerable discussion has ranged around the question whether the cutaneous manifestations of keratosi s blenorrahgia are on an infective or a toxic basis; most writers now favour the latter view. However, the occasional finding of Gram-negative intracellular diplococci in the lesions has confused the issue. Apart from theoretical interest the pathogenesis of this condition has 2 aspects of practical importance. First, the question of infectiousness of the purulent material of the crusts of the lesions raises the possibility of transmission of gonorrhoea to physician or nurse. Secondly, the effectiveness of local therapy depends on whether the disease is due to direct infection of the skin or is secondary to active foci elsewhere.

The author summarizes the findings under the following headings, consideration of which indicates a toxic process as being responsible for the cutaneous lesions of

keratosis blenorrhagica (i) The infrequency and inconclusiveness of the reports of cases in which the gonococcus was found in the lesions (ii) The simultaneous appearance of multiple lesions on widely separated areas of the body. (iii) The presence of oral lesions. (iv) The coexistence of admittedly toxic conditions of the eye. (v) The localization of the cutaneous manifestations to the same areas usually chosen by dermatophytids (vi) The response of the skin lesions to cure of the primary foci of the disease. (vii) The inefficacy of local therapy (viii) The complement-fixation test showing immunological changes in the body. (ix) The appearance of urethritis and arthritis prior to the development of the keratoderma. (x) In 90 per cent of the 75 cases the keratoderma first appeared during a relapse of a pre-existing urethritis and arthritis. This suggests that the first attack may sensitize certain portions of the skin in susceptible persons. The sensitivity of the skin disappears in 4 to 6 months and the lesions heal spontaneously.

Treatment

Fever therapy—F. C. Combes *et al.* report the results of the use of artificial fever in the treatment of keratosis blenorrhagica. They consider that this is the most effective method of treatment, and especially for patients so toxic and debilitated as to be unable to tolerate surgical treatment. In addition to improvement in the visible lesions and joints, there is a rapid favourable response, both mental and physical, such as cannot be obtained by any other method. Two cases were treated by means of inductothermy, in one, 3 treatments, at weekly intervals, of pyrexia reaching 106°F . for $3\frac{1}{2}$ hours, effected complete cure, in the other, cure resulted from 11 treatments, at 48-hour intervals, of pyrexia reaching 104°F ., lasting 3 to 4 hours.

Combes, F. C., Dietrich, C., and Cohen, J. (1940) *J. Amer. med. Ass.* **114**, 2078.

F Epstein, E. (1939) *Brit. J. Derm.*, **51**, 428.

GOUT

See also B.E.M.P., Vol. VI, p. 37; Cumulative Supplement, Key No. 579; and Surveys and Abstracts 1939, p. 359.

Aetiology

High Fat Diet

L. M. Loekie and R. S. Hubbard in 1935 showed that in a gouty subject a high fat diet provoked an acute attack and increased the content of uric acid in the blood. Further observations are now reported; the acute attacks thus excited may be accompanied by fever, often to 102°F ., and in the same individual the interval between the start of the diet and the provoked attack may vary from 2 to 16 days. P. S. Hench pointed out that these induced attacks of gout may occur during the usually 'immune period' following an ordinary attack, and that this effective provocative test might be useful (i) in deciding the diagnosis of gout, and (ii) in convincing a doubting, unco-operative patient that he has gout.

Common Factor in Gout and Rheumatism

In a paper on the relations of gout and rheumatism, acute and chronic, M. K. Sedláček of Prague brings forward arguments, chemical experiments, and observations on patients to show that gout, rheumatism, and several allergic states have a common, probably infective, origin. He describes a colloid protein substance isolated from the urine of gouty and rheumatic subjects, which is said to be formed in infective foci, and to be the cause of the gouty and rheumatic syndromes, rheumatism in youth, gout later in life. The composition of this substance appears to vary, but its parenteral injection is stated to exert a curative influence on a large number of morbid states—toxicoses, rheumatism, gout, and allergic conditions. The argument, not always clear, and the clinical observations, await confirmation.

Hench, P. S. (1939) *J. Amer. med. Ass.*, **113**, 1064.

Loekie, L. M., and Hubbard, R. S. (1939) *J. Amer. med. Ass.*, **113**, 1064.

Sedláček, M. K. (1939) *Acta Rheumatica*, **11**, 5.

Clinical Picture*Gout in Early Life*

According to P. S. Hench, gout in early life, like juvenile diabetes mellitus, is more severe than in patients first attacked in middle life, the disease advances more rapidly and with graver manifestations, and often proves fatal in the fourth decade of life.

Hench, P. S. (1939) *J. Amer. med. Ass.*, **113**, 1064

GRANULOMA, ULCERATIVE

See also B. I. M. P., Vol. VI, p. 54, Cumulative Supplement, Key No. 580, and p. 91 of this volume

Clinical Picture*Lesions of Cervix*

R. I. Arnell and J. S. Potekin described 38 cases of granuloma inguinale of the cervix. Four of the patients were white women in whom the condition is very rare. Most of the patients were between the ages of 20 and 40 years and only 2 of them were nulliparous. The condition usually gave rise to pelvic pain and a purulent or bloody discharge. Bleeding is due to ulceration of the tissue and occurred in 31 of these cases. In many patients cervical infection had existed before the granuloma became evident. In 5 of the cases ulceration was also present in the vulva. The diagnosis is made by demonstrating Donovan bodies in biopsy material. Treatment consisted of the intravenous injection of 10 c.cm. of a 1 per cent solution of tartar emetic, 2 or 3 times a week. Local therapy consisting of irrigation with potassium permanganate solution and the application of neoarsphenamine (4.5 per cent in glycerin) was also used. Large growths can be excised with the electro-cautery. In 17 cases the cervix was healthy after treatment. The granuloma is clinically easily confused with carcinoma of the cervix. There were 2 deaths from cervical haemorrhage in this series showing that the condition is by no means as innocuous as is sometimes supposed.

Arnell, R. I., and Potekin, J. S. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 626

HAEMATEMESIS

See also B. I. M. P., Vol. VI, p. 75, and Surveys and Abstracts 1939, pp. 47 and 360.

Aetiology*Due to Ingestion of Aspirin*

A. Hurst and G. A. M. Intott reported a case of haematemesis which they attributed to the ingestion of aspirin. This was a man, aged 57, admitted to hospital for repeated haemorrhages from the alimentary tract, generally in the form of haematemesis, but sometimes melaena only. Some years previously he had been treated for a gastric ulcer, though no X-ray or other investigations had been made. Three years afterwards he had had another severe haematemesis. Since the age of 18 he had suffered from severe migrainous headaches, for which he had been in the habit of taking at least 6 aspirin tablets a week, and often as many as 6 in a day. No X-ray evidence of a peptic ulcer could be found. A gastroscopy performed after 2 aspirin tablets, broken but not crushed, had been swallowed, showed within a few minutes that the mucosa adjacent to some larger fragments of the tablets became intensely hyperaemic and actual extravasation of blood occurred. A zone of hyperaemia developed around numerous smaller particles of aspirin. There appeared to be no doubt that this was a case of extreme sensitiveness to aspirin; and the intensity of the reaction produced was sufficient to warrant the belief that aspirin was the predominant and perhaps the sole factor responsible for the repeated bleeding.

Hurst, A., and Intott, G. A. M. (1939) *Gen. Hosp. Rep.*, **19**, 173

HAEMATOPORPHYRINURIA

See also B.I.M.P., Vol. VI, p. 85, and Surveys and Abstracts 1939, p. 361.

Biochemical*Chemistry of Porphyrins*

C. Rimington described the chemistry of the porphyrins which are essentially similar in structure to bilirubin. From the biological point of view protoporphyrin is the most important of them because when combined with iron it forms haematin. The porphyrins are widely distributed in nature, in plants, in some bacteria such as the diphtheria bacillus and in small quantities in the erythrocytes in the blood. They are also present in bile, faeces, and normal urine. Porphyrin excretion may be markedly increased in certain pathological conditions. It may occur in hepatic insufficiency, in toxæmia from drugs of the sulphonamide group and antipyretics, and in plumbism. Congenital porphyria is characterized by the excretion of large amounts of copro- and uro-porphyrins. Uroporphyrin is also deposited in the bones and teeth giving them a deep brown colour. The patients are very photosensitive, but suffer from no other disability from their condition. Acute idiopathic porphyria sometimes occurs, usually at the age of about 30 years. There are repeated attacks of porphyrinuria, severe abdominal colic, and obstinate constipation. Later nervous or neuro-muscular symptoms develop followed by paralysis and death. Photosensitivity is absent and there is no discoloration of the bones. According to Waldenström the condition is inherited as a Mendelian dominant.

Rimington, C. (1939) *Proc. R. Soc. Med.*, **32**, 1268.

Waldenström, J. (1937) *Acta med. scand.*, Suppl., p. 87.

Clinical

F. G. Chandler *et al.* defined clinical porphyrinuria as a state of porphyrinuria which changes the colour of the urine. This definition was adopted because porphyrinuria which does not do this is seldom of clinical importance. They gave an account of the chemistry and classification of the porphyrins. The condition may be congenital, acute idiopathic, or due to drugs such as sulphonal. The signs and symptoms vary in the different forms. The urine is red from birth in the first, in adult life in the second, and after taking large amounts of the drug in the third. Photosensitivity and pigmentation of the bones and teeth are present only in the congenital type. Abdominal and other toxic symptoms are present only in the other two types. The congenital variety occurs mostly in males and the other two mostly in females. In a case of acute idiopathic porphyrinuria, the patient had red urine, pigmentation of the skin, vomiting, intense abdominal pain, and loss of weight. The patient died after about 3 years' illness. The authors described simple and more complicated tests for detecting porphyrin in the urine and ascertaining its exact composition. They stressed the importance of not subjecting idiopathic porphyrinurics to unnecessary laparotomy in an attempt to find the cause of the abdominal pain and vomiting.

Acute Porphyria without Porphyrinuria

I. Schie describes a case in a female aged 35, of that very rare disease, acute porphyria, which is a disorder of pigment metabolism and has some connexion with haemoglobin synthesis. The patient showed all the symptoms of a mechanical ileus. On laparotomy the colon was markedly dilated, whereas the small intestine was completely collapsed, no obstruction could be found. The urine was dark, but did not contain porphyrin. The appearance of porphyrin is usually the most obvious symptom of the disease. The patient's urine contained, however, pigments which were similar to those usually accompanying porphyrinuria. Examination of the patient's relatives and their history proved negative as regards porphyrinuria. The findings at necropsy were not very conclusive. The kidneys were small and contracted, and showed chronic interstitial nephritis with degenerative and vascular changes. The liver, which is supposed to be the site of the transformation of porphyrin, showed degenerative changes.

Porphyrin Excretion following Antipyretics

G. Brownlee stated that the toxic symptoms following the use of coal-tar antipyretics and the chemically related drugs of the sulphonamide group were due to the oxidation of the aromatic amino group of compounds. Other investigators showed that porphyrinuria occurred in rats after the oral administration of sulphanilamide. Brownlee investigated the porphyrin content of the urine of rats after they had received antipyretics of the coal-tar group by mouth. He found that, depending on the dose and solubility of the drug used, the excretion rose slowly to a maximum in 9 days. Phenacetin and phenazone produced the same degree of porphyrinuria, amidopyrine and aspirin were twice as potent, acetanilide four times, and *p*-aminophenol even more potent than acetanilide. These results were exactly parallel to the acute toxicity of the drugs. If given for some time the drugs destroyed erythrocytes. Other workers have found that the methaemoglobin produced by these drugs is formed by the oxidation of haemoglobin by *p*-iminoquinone which is formed. This is reduced to *p*-aminophenol which is then oxidized to *p*-iminoquinone and the process repeats itself. It is thought that the production of these substances accounts for the therapeutic action of the drugs of the coal-tar antipyretic and sulphanilamide groups. It was suggested that the amount of porphyrinuria present might be used as an index of toxicity in the therapeutic use of these drugs.

Porphyrinuria with Psychotic Symptoms

H. Roger *et al.* report a case of porphyrinuria with psychotic symptoms. An 18-year-old boy had psychotic symptoms of hebephrenic type and also a porphyrinuria with the typical skin eruptions of this symptom-complex and with photosensitivity. He had a slightly enlarged liver and spleen, and signs of a latent liver insufficiency; the coagulation time of the blood was 12 minutes, these facts indicate, in the authors' view, that the cause of the porphyrinuria might be hepato-splenic. As a rule the nervous manifestations of porphyrinuria are not accompanied by skin eruptions, and the symptoms are on the whole more neurological (Lindry's disease) than psychotic. This case seems to be the first to be reported in which a porphyrinuria is combined with a psychosis of the 'fugue' type. The case is classified as a mixed cutaneous-nervous porphyrinuria. Treatment with nicotinic acid was unsuccessful.

Brownlee, G. (1939) *Proc. R. Soc. Med.*, **32**, 1276.

Chandler, F. G., Harrison, G. A., and Rimington, C. (1939) *Brit. med. J.*, **2**, 1173.

Roger, H., Paillas, J.-F., Boudouresques, J., and Schachter (1939) *Bull. Soc. med. Hop. Paris*, **55**, 1145.

Schie, I. (1939) *Acta med. scand.*, **62**, 618.

HAEMATURIA

See also B.I.M.P. Vol. VI, p. 97, and Surveys and Abstracts 1939, p. 361.

Aetiology*Sulphapyridine Therapy*

Y. F. Tsao *et al.* report 5 cases of haematuria following sulphapyridine treatment, all in children, who did not receive large doses of the drug for their age and weight. In one case the haematuria appeared within 20 hours of the onset of treatment. One of the children died of uraemia due to bilateral ureteric obstruction by concretions, which are probably the cause of the haematuria in all cases. Children should be treated with sulphapyridine with great care because they are probably more susceptible to renal complications. If signs of renal failure occur, every attempt should be made to relieve the obstruction.

Tsao, Y. F., McCracken, M. F., Chen, F., Kuo, P. T., and Dale, C. L. (1939) *J. Amer. med. Ass.* **113**, 1316.

HAEMOPHILIA

See also B.E.M.P., Vol. VI, p. 123, and Surveys and Abstracts 1939, p. 361

Aetiology*Delayed Formation of Thrombin*

K. M. Brinkhous supports the view that the clotting defect in haemophilia is due to a defect in one or more of the factors concerned in the formation of thrombin. In 5 cases of haemophilia he found that the prothrombin and fibrinogen contents of the plasma were normal. The antithrombic activity of the smear and plasma and the ability of thrombin to clot the haemophilic plasma were also normal but the rate of thrombin formation from prothrombin was 30 times higher in the normal than in the haemophilic blood. This slow formation of thrombin in haemophilia allows it to be destroyed by antithrombin almost as soon as it is formed. Adding organ extracts rich in thromboplastin in as little as 1 mg. of extracted material to 100 c.cm. of haemophilic blood produced a normal prothrombin conversion rate. It is suggested that the platelets in haemophilia contain a normal amount of thromboplastin, but liberate it very slowly. Blood transfusion restores the clotting time of the haemophilic to the normal and it remains so for many hours. It is suggested that this is because thromboplastin is supplied from the cells and platelets of the donor's blood.

Brinkhous, K. M. (1939) *Amer. J. med. Sci.* **198**, 509

Incidence*Sex Ratios in Families*

It has been stated that the children of transmitters of haemophilia are more often male than female. Other observers have asserted that the opposite holds true. The usual sex ratio in most countries is 106 males to every 100 females born. Madge T. Macklin analysed the sex ratio in 2,211 reported haemophilic families. On v those were considered in which the number and sex of all children born in the one generation was given. The children of female carriers of haemophilia and those of haemophilic males are included. The proportion of males to females in the families of transmitters was 58.3 to 41.7. The excess of males is probably because transmitters are only recognized when they have male children who develop the disease. In the families of haemophilic males the proportion of males to females was 45.7 to 54.3. These figures are well within the limits of the normal and it was concluded that the normal sex ratio is not altered in the children of haemophilic families.

Macklin, M. T. (1939) *Amer. J. Dis. Child.* **58**, 1215

Clinical Picture*Coagulation of Blood Plasma*

H. Dam and H. Vennedt compared the ability of tissue extracts to coagulate haemophilic plasma with their ability to coagulate normal plasma. Extracts of human brain and other organs were used. In the presence of small quantities of the extract, haemophilic plasma did not coagulate so readily as the normal. In the presence of large quantities, however, the coagulation times were the same. If platelet suspensions were used instead of tissue extracts these differences between the coagulation times of the two plasmas became even more marked. These results may occur because the small quantity of tissue extract is neutralized by the haemophilic plasma or because some substance is lacking in it.

Dam, H., and Vennedt, H. (1940) *Lancet*, **1**, 70

HAEMORRHAGIC DISEASES

See also B.E.M.P., Vol. VI, p. 138, Surveys and Abstracts 1939, p. 362; and pp. 16 and 31 of this volume

Purpura Haemorrhagica*Following Arsenical Therapy*

D. Robertson Gorrie reported 21 cases of purpura haemorrhagica following arsenical treatment, 1 case, reported in detail, occurred in a man aged 30 years

who had had 7 injections of neoarsphenamine in the treatment of syphilis. Two years previously he had also received the drug for the same condition with no untoward results. On the second occasion he developed gross haematuria and skin petechiae. A necrotic angina occurred in the throat leading to a provisional diagnosis of diphtheria, but on examination no organisms were found. Blood examination showed thrombocytopenia, leucopenia, and normocytic anaemia. No vitamin-C deficiency was demonstrable. The patient was treated with vitamin P (0.25 g. of hesperidin every 2 hours by mouth) and a blood transfusion, and made a good recovery.

Gottlie D. R. (1940) *Lancet*, **1**, 1005

Hypoprothrombinaemia

Treatment

Synthetic vitamin-K substitute J. L. Rhoads and M. T. Hiegelman employed 2-methyl-1:4-naphthoquinone, a synthetic vitamin-K substitute, in 10 patients with prothrombin deficiency, including cases of carcinoma of the pancreas and of the colon, icterus gravis, obstructive jaundice, and haemorrhagic tendencies in the newly-born. In 9 cases a satisfactory response was obtained, though 3 of these cases had failed to respond satisfactorily to various forms of vitamin K. Seven of the cases responded to an oral dose of 1 mg. of the synthetic vitamin per day, in 6 cases the prothrombin time returning to normal within 24 hours of the initial dose. In 2 cases the daily dosage was 4 mg. All the patients received bile salts, in the form of iron bile salts, 0.6 to 2.0 g. per day, or sodium desoxycholate, 0.015 to 0.40 g. per day. The authors stated that 2-methyl-1:4-naphthoquinone appeared to be the most potent agent so far employed clinically for the treatment of prothrombin deficiency.

Synthetic vitamin K—W. De W. Andrus and J. W. Lord report that the intramuscular injection of 2-methyl-1:4-naphthoquinone in corn oil is a simple and effective means of restoring the plasma prothrombin level in the absence of severe liver damage. Single injections of as little as 2 mg. restore the plasma prothrombin level by as much as 48 per cent, and the effect of the drug is evident as early as 8 hours after injection. The effect of a single injection may be prolonged over a week, unless adverse factors, such as operations on the biliary tract or other liver damage supervene. No toxic effects have been observed by the authors following doses as high as 4 mg.

R. Kark and A. W. Souter assessed the value of synthetic vitamin K in the treatment of hypoprothrombinaemia. When there was no evidence of severe hepatic lesion the synthetic vitamin quickly restored the prothrombin level to normal. In 9 out of 18 cases 1 to 6 c.c.m. of the vitamin restored the level rapidly to normal. In 3 patients who had suffered from haemorrhage the level was quickly raised by giving the drug intravenously or intramuscularly. In 12 patients with liver disease, neither the synthetic vitamin K nor that derived from alfalfa had any effect upon the lowered prothrombin level.

Andrus, W. De W., and Lord, J. W., Jr. (1940) *J. Amer. med. Ass.*, **114**, 1336.

Kark, R., and Souter, A. W. (1940) *Lancet*, **1**, 1149.

Rhoads, J. F., and Hiegelman, M. T. (1940) *J. Amer. med. Ass.*, **114**, 400.

Haemorrhagic Diseases of the New-Born

A. J. Quick and A. M. Grossman investigated haemorrhagic disease of the new-born. They gave an historical survey of the condition from Biblical times up to the discovery of prothrombin deficiency and the importance of vitamin K, which put the whole question on a new level. Using Quick's method of determination they found the blood prothrombin level high in a small series of new-born infants. It was about 60 to 75 per cent of the normal adult value. The level, however, dropped during the first day of life, was slightly higher on the second day, and usually returned to normal on the third. Quick and Grossman concluded that all new-born infants are therefore in danger of haemorrhagic disease during the first day of life. The recovery of the prothrombin level to normal is thought to be due to the synthesis of vitamin K by bacteria in the intestine. The delay of this synthesis is suggested

as the possible cause of haemorrhagic disease of the new-born. The condition, which is sometimes fatal, can always be cured by giving vitamin K by mouth.

Quick, A. J., and Grossman, A. M. (1940) *Amer. J. med. Sci.*, **199**, 1.

Thrombocytopenic Purpura

Reaction of Peripheral Blood and Bone Marrow

L. R. Limarzi and E. M. Schleicher investigated the reaction of the peripheral blood and bone marrow to acute and chronic haemorrhage and in essential thrombocytopenic purpura. Five normal men, 5 normal women, 6 patients with thrombocytopenic purpura, 3 with symptomatic purpura, and 5 with chronic haemorrhage were investigated. The authors found that acute haemorrhage caused hyperplasia of the bone marrow which rapidly returned to normal. In chronic haemorrhage there was a similar hyperplasia, but the megakaryocytes were not all of the adult type, intermediate forms being present. Platelets were present in large numbers in both the marrow and the peripheral blood. When the haemorrhage ceased, the blood returned to normal. In essential thrombocytopenic purpura with haemorrhage there was a similar hyperplasia. In the more chronic forms myeloid and erythroid hyperplasia might not occur, but there was usually megakaryocytic hyperplasia, the adult types of these cells appearing in the more chronic forms. Platelets were reduced in the bone marrow and the peripheral blood. The megakaryocytes did not mature properly in this condition but, if the spleen was removed, the bone marrow returned to normal. It is possible that the condition is due to elaboration in the spleen of some factor which prevents proper maturation of these cells. In symptomatic purpura the blood platelets were normal. The megakaryocytes in the bone marrow were increased in number but not so greatly as in essential thrombocytopenic purpura. The bleeding and coagulation times of the blood were normal and a normocytic anaemia was present. The purpura was due to disease of the capillaries.

Platelet-reducing Extracts from Spleen

I. C. G. Hobson and L. J. Wits investigated the observation, already criticized, of Troland and Lee (1938) that an extract from spleens removed from patients with thrombocytopenic purpura reproduced the condition in animals. A spleen, weighing 250 g. and removed from a woman, aged 48, with all the clinical features of thrombocytopenic purpura, was extracted with acetone for 17 days and, after removing the latter, and making up the extract to 100 c.c.m. with distilled water, 5 c.c.m. and 20 c.c.m. respectively were injected intravenously into 2 rabbits. Little effect was produced by 5 c.c.m., but after 20 c.c.m. there was a sharp fall in the number of platelets. Another 45 c.c.m. were then injected into the first rabbit, and the platelets fell in 30 hours from 525,000 to 109,000 per c.c.m., returning to normal by the fifth day. The injection of 40 c.c.m. of an acetone extract of normal spleen into a third rabbit produced in 2 hours a fall in platelets from 454,000 to 306,000 per c.c.m.; return to normal occurred within 24 hours. An extract of normal spleen in Ringer's solution was also employed and found to be more effective than the acetone extract of normal spleen. The authors concluded that, before comparing the effects of extracts of thrombocytopenic spleens, the optimal conditions for extracting platelet-lowering substance from normal spleens should be determined.

Hobson, I. C. G., and Wits, L. J. (1940) *Brit. med. J.*, **1**, 50.

Limarzi, L. R., and Schleicher, E. M. (1940) *J. Amer. med. Ass.*, **114**, 12.

Troland, C. I., and Lee, F. C. (1938) *Johns Hopk. Hosp. Bull.*, **62**, 85.

(1938) *J. Amer. med. Ass.*, **111**, 221.

HAEMOTHORAX

See also B.E.M.P., Vol. VI, p. 156.

Spontaneous Haemothorax

M. Davidson and C. K. Simpson reported spontaneous haemothorax in an apparently healthy man aged 26. Necropsy showed an apical bulla associated with healed apical tuberculosis, which had ruptured spontaneously, causing sudden

pneumothorax, the latter in turn had stretched and torn basal adhesions leading to slow and continuous haemorrhage

Davidson, M., and Simpson, C. K. (1940) *Lancet*, **1**, 547.

HAIR FOLLICLES, ABNORMALITIES AND DISEASES

See also B F M P., Vol. VI, p. 162, and Surveys and Abstracts 1939, p. 363.

Epilation

M. Lapiere and M. Dumont reported on 100 cases of epilation effected by thallium acetate and X-rays. Thallium acetate alone had drawbacks, but in reduced doses used in conjunction with X-rays it was the optimal treatment even in resistant cases. The X-ray dose must be small and very carefully administered; there is no fear of dangerous side-effects.

Lapiere, M., and Dumont, M. (1939) *Bull. méd.*, **19**, 1189.

Pili Torti

I. F. Hellier described a case of pili torti, or twisted hair, a rare congenital abnormality not previously described in Great Britain. Clinically, the condition resembles monilithrix, with short broken hairs appearing in childhood. On microscopical examination, however, the hairs are not beaded, but are flattened and, at irregular intervals, completely twisted round their long axis through 180°. The condition can be diagnosed by the naked eye, once a case has been seen. The hairs are broken and short, especially over the occipital region. The most characteristic feature is a peculiar spangled glint, due to the unequal reflexion of light from the twisted hair. On examining the hair microscopically, the periodic torsions are readily seen. The twisting is not present at birth, but is generally seen between the ages of one and two. The condition is commoner in females. It has been suggested that the hair becomes practically normal after puberty. In the case reported, epilation with thallium acetate, and, later, the application of a slightly alkaline lotion, was followed by some improvement.

W. I. Astbury and I. O. Bell examined Hellier's case of pili torti by means of X-rays to discover whether the deformity of the hair shaft was associated with any detectable molecular disturbance. Neither pili torti nor monilithrix showed any molecular disturbance recognizable by X-ray diffraction as a departure from the familiar keratin type of structure. Even the histological irregularity was by way of being only a spasmodic variation of the normal. The causative mechanism appears to be associated partly with a curvature in the follicle, and partly with rhythmic rotatory movements of the latter. The fact that polarized light reveals internal malformation in apparently unaffected lengths of hair-shaft indicates that the growth mechanism is at fault almost continuously.

Astbury, W. I., and Bell, I. O. (1940) *Brit. J. Derm.*, **52**, 176.

Hellier, I. F. (1940) *Brit. J. Derm.*, **52**, 173.

Hirsutism

Treatment

Endocrine therapy.—G. B. Doiff employed endocrine therapy in a group of 8 females, from 15 to 23 years of age, who showed varying degrees of hirsutism, from slight facial and bodily hair growth to such marked hair growth that it required shaving, and who showed, in addition, some enlargement of the clitoris and some menstrual irregularities. In 3 cases inunction of the face with an ointment containing oestrogen produced a very slight bleaching effect in the area treated, and sometimes a breaking-off of hairs. No such effect was noted in areas to which the ointment was not applied. In one case combined inunction and injection of oestrone produced the same bleaching effect, and also an actual loosening and falling out of some of the hair on the thighs. In 2 cases the oral administration of emmenin (placental extract containing both oestrogenic and gonadotrophic substance) combined with local and hypodermic oestrogenic therapy provoked loosening of superfluous hair,

this effect was more dependable and more prompt than that of oestrogenic substance. Though a regrowth of hair occurred later, this was lighter in colour and finer in texture. No effect occurred on normal hair. The author felt that this subject calls for further investigation.

Dorff, G. B. (1940) *Ann intern Med* **13**, 2112

HAND, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. VI, p. 171.

De Quervain's Tenosynovitis

Treatment

Cassart reports on the treatment of de Quervain's tenosynovitis, which is characterized by a painful creaking of the abductor tendons of the pollicis longus and brevis muscles. In the early stages there is proliferation of vascular connective-tissue, and physiotherapy, as often practised, has no effect. Immobilization in a plaster, preferably in plaster-of-Paris, for 3 weeks followed by 2 weeks' rest are necessary to treat the condition satisfactorily. Surgical treatment is only necessary in the later stages when fibrosis prevents the regression of early proliferation, in these cases the tendon sheath must be opened and the tendon liberated. The author disagreed with the usual view that the condition only appears in the fourth decade, his patients were all well under this age.

Cassart (1939) *Sculpel, Laëge*, **92**, 884

HEADACHE

See also B.L.M.P., Vol. VI, p. 199, Cumulative Supplement, Key No. 618; and Surveys and Abstracts 1939, p. 363

Types of Headache

Due to Ovarian Insufficiency

R. T. Guiral examined 30 female patients who had suffered from intense headache for a long time. They were fairly fat and had some disturbance of menstruation. A constant localization of headache was not observed or anything abnormal in the nervous system except a slight defect in the visual fields of the upper temporal quadrant, sometimes affecting also the lower temporal quadrant. Hyperactivity of the pituitary was diagnosed, resulting from ovarian hypofunction. To these patients 20,000 to 50,000 units of folliculin were given every week. The headache disappeared in all cases, sometimes after an exacerbation of pain at the beginning of treatment lasting some days or weeks, and the visual fields became perfectly normal.

Guiral, R. T. (1939) *Arch. Méd. Enf.*, **5**, 182

HEART DISEASES: EXAMINATION

See also p. 98 of this volume.

Cardiac Examination of Recruits

Thomas Lewis in the second edition of *The Soldier's Heart and the Effort Syndrome* writes with the mature experience of the last war and since, and shows that the state variously described in the past and now known as effort syndrome has been a preventable loss of huge dimensions, nearly half the patients invalided for this condition had the symptoms before joining the forces, and more than half developed them before their training was complete. This was due to failure of the recruiting boards to eliminate most of those men, because it was not realized that the stethoscope, though it may detect some of the unfit, can never prove soundness of health or even of the heart or lungs. The simple conclusion was slowly reached that capacity for work is most certainly determined by watching men when at work, a method of examination which would have been more efficiently carried out by instructors of physical training on the parade ground. During the 1914-18 war, especially during the last 2 years, exercise tests were more often used, but recently

unsuitable men have been taken by the services in numbers because tolerance tests have not been properly applied. The three reasons given why full exercise tests are neglected are (i) their great value is not appreciated, (ii) they are supposed to take up too much time, and (iii) they are erroneously thought to be risky, and they are shown to be fallacious. The preliminary examination by the medical man is on much the same lines as that for life assurance or pension purposes and is specially intended to detect undefined ill-health and cardiac cases. The chief signs indicating serious cardiac disease in recruits are breathlessness at rest, over-distension of the veins of the neck, definite cardiac enlargement, irregular action with fast heart rate, an early diastolic murmur to right or left of the sternum, a diastolic rumble at the impulse, a basal or apical thrill, and a blood-pressure of 180 mm Hg or over at rest.

Test exercises are not necessary for men found to show signs warranting rejection in the preliminary examination. The first and most important duty of members of recruiting, discharging, and pensioning boards is to familiarize themselves with the reaction of the body to test exercises in health and disease. The preliminary exercises, which are perfectly safe, are (i) to walk briskly up 40 stairs, taking one at a time, (ii) to hop 20 times easily on each foot, raising the shoulders 6 inches at each hop, and (iii) to step up on to a 15 to 18 inch chair 20 times (in 60 seconds), coming upright each time. The subject may use the back of the chair to steady himself. The best of these is the stair test, because it is the most customary form of exercise, but the most convenient should be used, and only one of the three. A healthy man leading a sedentary life shows little respiratory reaction to any of these tests, the pulse rises 20 to 25 beats a minute, but returns to its original rate within 1½ minutes, the respiratory response is more important than that of the pulse. Any man whose breathing is obviously disturbed, or whose pulse rises by more than 30 beats and falls slowly has a poor exercise tolerance and should not be passed into Grades I, II, or III without re-examination and then usually into Grades III or IV. The response may be increased by infections, such as a common cold. The preliminary test fails to weed out many recruits with serious cardiac mischief or effort syndrome, and therefore must be followed by a more strenuous test.

The final test is always safe in men who have passed the preliminary test, and men who state that their wind is good may proceed to it without being submitted to the preliminary test. *Its object is to produce breathlessness*, and the gauge of tolerance is the amount of exercise taken. A weight of 20 lb (10 for a woman) is raised from an inch above the floor to the full extent of the arms above the head, the arms being raised in an easy movement at the rate of one lift in 2 seconds. A healthy young man of sedentary habit can repeat this lift 30 or 60 times, but at the end will be breathless and be seen to have laboured breathing. An athlete in training will continue much longer without complaint. Unhealthy subjects (effort syndrome, cardiac and respiratory cases) will become distressed before 20 lifts have been made, and no man who cannot make 20 lifts is fit for Grades I or II, those who cannot make 30 lifts should be recommended for graduated training. Most men who make more than 30 lifts are fit for Grade I. Occasionally cases of quite uncomplicated mitral stenosis or early aortic regurgitation pass this final test and may give a good deal of useful service, but they should not be recruited except in the gravest emergency.

Parkinson writing on cardiac examination in wartime, while fully recognizing the value of symptoms in diagnosis, for example in angina pectoris, considers that the recognition of slight cardiac disease in men of military age should be approached by a very different method, here physical signs become the basis of diagnosis. Unfortunately, these may be slight, dubious and difficult to interpret, and a shaky sign is a poor foundation for a weighty diagnosis. The work of a medical examiner in war-time is difficult, and constant care can hardly prevent the occasional acceptance of unsuitable recruits, which are almost confined to rheumatic and perhaps congenital heart disease. The medical history of the candidate must receive due attention, but a record of tonsillitis is of little value, and of scarlet fever or diphtheria almost none. The appearance only helps if there is cyanosis with clubbed fingers in congenital morbus cordis, and the colour of the cheeks varies so much in health that the suspicion of mitral disease should not easily be aroused. Pulse-response tests (so-called exercise tolerance tests) can have little value in the recognition of myocardial or valvular disease, or indeed in the assessment of

myocardial efficiency, though they are valuable in judging the nervous control of the heart. A medical examiner soon recognizes the natural rapid pulse of nervousness, persistent tachycardia may be due to fever or a neurosis, or toxic goitre and depend on the nervous rather than on the cardiovascular system. The normal sinus arrhythmia and the fact that extrasystoles disappear with quickened pulse rate of a trial exertion must be borne in mind. The apex beat is a more reliable clinical guide to the diagnosis of cardiac enlargement than is percussion which is waste of time in early or doubtful cardiac disease. Though the apex beat may not be palpable, this makes cardiac enlargement unlikely. A diffuse apex beat is not evidence of enlargement. Outward displacement is rare unless the heart is enlarged. In auscultation it is generally better not to listen too long, but to pause and try again, and the stethoscope should fit loosely in the ears, for, if tight hearing is dulled. Mitral stenosis should never be diagnosed on a sudden (or snapping) first sound alone, and exertion should be induced to bring out a presystolic murmur. A systolic murmur at the base of the heart may generally be ignored if soft and obvious only in recumbency. A systolic murmur at the apex gives more trouble, and no diagnosis is satisfactory which depends on its presence. If at all difficult to hear being soft and short, if louder at the end of inspiration, if varying much with posture, it is probably functional and can be neglected. Anaemia is a frequent cause of systolic murmurs, basal and apical. But an apical systolic murmur may be a clinical hint of aortic incompetence. The secret of the diagnosis of aortic regurgitation in an early stage is the detection of the diastolic murmur, the collapsing pulse and the capillary pulsation of the fully developed disease may be forgotten.

Lewis, T. (1940) *The Soldier's Heart and the Effort Syndrome*, pp. 82-91, London.

Parkinson, J. (1940) *Brit. med. J.*, **1**, 428.

HEART DISEASES. CONGENITAL DISEASES

See also B.F.M.P., Vol. VI, p. 206, Cumulative Supplement, Key Nos. 619-635, and Surveys and Abstracts 1939, p. 364.

Congenital Idiopathic Hypertrophy of Heart

B. Benjamin and M. A. Simon reported a case of so-called congenital idiopathic hypertrophy of the heart occurring in a child aged 4 months. The patient had never thrived since birth, vomiting being a marked feature of her condition. She was admitted to hospital because of restlessness, vomiting, and coughing. The cardiac dullness was greatly enlarged and air entry diminished on the left side of the chest. There was some cyanosis of the extremities, and the infant was undernourished. She became worse, with more cough and cyanosis, and finally died 35 hours after admission. Necropsy showed an enormous heart which had compressed, and caused collapse of, the lower left lung. The condition was probably due to a low-grade, non-specific pericarditis. The heart showed marked endocardial fibrosis, epicardial thickening, and adhesions, and perivascular fibrosis. Most cases of so-called congenital hypertrophy of the heart show some pathological lesion.

Benjamin, B., and Simon, M. A. (1940) *Amer. J. Dis. Child*, **59**, 842.

Heart-Block

G. M. Currie described a case of complete congenital heart-block in a child of 2 years. The postulates for accepting the diagnosis of the condition are recognition in early life, absence of any illness previously which could have caused the condition, e.g. diphtheria, rheumatism, or syphilis, and lastly electrocardiographic demonstration. The presence of congenital heart disease lends weight to the diagnosis. The child had had several typical Stokes-Adams attacks lasting, at the most, a few minutes. The heart was enlarged laterally in both directions, the precordium bulged, and there was a thrill associated with a harsh loud systolic murmur in the front left interspace just inside the nipple which is associated with a patent interventricular septum. No other abnormality was found. The electrocardiogram showed a complete heart-block with an auricular rate of 111 and a ventricular rate of 38 per minute. After the injection of 0.5 gr. of atropine sulphate a 3:1

partial block resulted. Since 16.5 gr produced only an approximation to a 4:1 block, the effect was thought to be coincident rather than a pure production of a partial block.

Currie, G. M. (1940) *Brit. med. J.*, **1**, 769.

HEART DISEASES RHEUMATIC HEART DISEASE IN CHILDREN

See also B.L.M.P., Vol. VI, p. 234, and Surveys and Abstracts 1939, p. 365.

Clinical Picture

Heart Lesions

T. I. Bland and T. D. Jones report an investigation showing that during the course of acute rheumatic fever nearly 70 per cent of the patients are left with cardiac involvement. Of 1,000 patients, 314 (31 per cent) on recovering from rheumatic infection did not show any evidence of cardiac disease, but of these 314 patients followed up for 10 or more years, 79 (25 per cent) showed signs of permanent valvular deformity. In two-thirds of the patients the heart signs appeared with a recurrence of the rheumatic fever, and chorea was very common. In the remaining third the onset of heart disease was insidious, but was probably associated with persistent subclinical rheumatism. It is concluded that in patients recovering from the original attack without any cardiac lesions who during the second decade of life are still free from cardiac involvement, the risk of a heart lesion developing later becomes more remote.

Bland, T. I., and Jones, T. D. (1939) *J. Amer. med. Ass.*, **113**, 1380.

Diagnosis

H. Robbins and M. H. Durante pointed out that, in acute rheumatic carditis, an erroneous diagnosis of pneumonia may easily be made because of the passive pulmonary congestion often accompanying rheumatic carditis. In these cases the lungs show slight or marked dullness just below the angle of the scapula in addition to diminished breath sounds and occasionally moist rales. These lung findings in the presence of a high temperature and dyspnoea may easily be mistaken for pneumonia. To avoid this error it is necessary first to recognize the presence of rheumatic carditis, which may be done by obtaining a history of joint pain accompanied perhaps by an upper respiratory infection and coupled with evidence of cardiac involvement. The increased blood sedimentation rate will furnish additional evidence.

Robbins, H., and Durante, M. H. (1940) *Arch. Pediat.*, **57**, 216.

HEART DISEASES PERICARDIUM DISEASES

See also B.L.M.P., Vol. VI, p. 256, and Surveys and Abstracts 1939, pp. 58, 60, and 365.

Chronic Constrictive Pericarditis (Pick's Disease) with Calcification

C. I. Drummond reported a case of chronic constrictive pericarditis with calcification. An unusual symptom in this case was that the patient's head and neck became oedematous in the morning, the oedema subsiding after the patient had sat up for a few hours. At necropsy about a pint of fluid was found in the right chest cavity. The heart was small and covered by a dense calcified pericardium, firmly adherent to the myocardium and great vessels.

Drummond, C. I. (1940) *Northw. Med., Seattle*, **39**, 217.

HEART DISEASES. MYOCARDIUM DISEASES

See also B.F.M.P., Vol. VI, p. 277; and Surveys and Abstracts 1939, p. 367

Subacute Myocarditis of Unknown Aetiology

D. Magner records the case of a woman, aged 50, who for 30 years had been first as nurse and then as a laboratory technician in a tuberculous sanatorium, and had had haemoptysis on at least two occasions. Eighteen hours after a subtotal removal of a simple colloid goitre she suddenly died, no evidence of cardiovascular disease or recent acute infection having been found before operation. The myocardium showed numerous focal lesions with disappearance of the muscular fibres and the presence of plasma cells, macrophages, and giant cells resembling true foreign-body giant cells. Specially stained sections did not show spirochaetes, acid-fast bacilli, or other bacteria. The liver showed small pale areas of recent focal necrosis without inflammatory reaction, and in the right caudate nucleus of the brain there was an old focal necrosis, approximately 1 mm. in diameter, with surrounding patchy gliosis. The lesions were not regarded as due to tuberculosis, syphilitic or rheumatic infection, or to sarcoidosis. A. R. Rich, who examined the sections, had seen 6 other cases precisely identical and without any constant association with active tuberculosis, syphilis, or rheumatic fever, and Jonas, also of the Johns Hopkins Hospital, recently described 5 cases of granulomatous myocarditis, presumably some being those mentioned by Rich.

Jonas, A. F. (1939) *Johns Hopk. Hosp. Bull.*, **64**, 45

Magner, D. (1939) *Amer. J. med. Sci.*, **198**, 246

Gonococcal Myocarditis

O. Bang of Copenhagen reports 6 cases of myocarditis in which there was strong evidence of gonococcal origin. These cases were met with in the same hospital within one year. The diagnosis was made on the grounds that all the 6 patients showed electrocardiographic changes in the course of acute or chronic complicated gonococcal infection. In some cases the myocarditis was slight and transitory, but in 2 cases there was persistent incomplete bundle-branch block, and in a third patient considerable anginal pain was still troublesome when he was re-examined a year later. Probably this condition often escapes detection, because suggestive symptoms may be absent. Since the use of the complement-fixation test was employed as a routine in cases of acute arthritis a high proportion of cases of supposed rheumatic fever have been shown to be really gonococcal arthritis, and it seems a priori not improbable that some cases of 'rheumatic' heart disease are gonococcal, and that the same is true about some instances of chronic 'degenerative' heart disease. At present, apart from acute gonococcal myocardial involvement in the bacterial endocarditis of gonococcal origin, myocarditis is seldom recognized as due to gonococcal infection. The article gives a number of useful references to gonococcal myocarditis.

Bang, O. (1940) *Brit. med. J.*, **1**, 117.

Foreign Bodies in Heart and Pericardium

H. R. Decker reviews 109 collected cases of foreign bodies in the heart and pericardium, including 23 cases of migrating foreign bodies, 9 of which had passed into the arterial circulation. The important decision is whether or not to remove the foreign body and, if so, when it should be done. He reports a case of a bullet lying close to the diaphragm and pericardium, which produced painful symptoms and a psychoneurosis. At first removal was recommended, but the patient improved, and for 7 or 8 years has been free from symptoms. The condition may be symptomless, but pain, asthenia, dyspnoea on exertion, and neurotic reactions are common. Physical signs may also be absent. In this series there was a mortality of 17 per cent after operation, and of 30 per cent in those not operated upon. As 6 deaths in the last group were not specifically the result of the heart injury, it was concluded that when all series were averaged the mortality for both operation and non-operation was about 20 per cent. A sharp or large foreign body should be removed, and it is relatively safe to remove foreign bodies in the pericardium. Untoward cardiac

symptoms during operation indicate that it should be abandoned. Intramural fixed bodies as a rule do not cause death or shorten life. After the foreign body is removed the symptoms it caused usually disappear.

Decker, H. R. (1939) *J. thorac. Surg.*, **9**, 62.

Stab Wounds of the Heart

C. B. Olim and J. D. Hughes record a case of heart wound in which it was necessary to ligate the anterior coronary artery. The wound was in the left ventricle about 2 cm. to the left of the anterior descending coronary vessels and 5 cm. from the apex. As it was impossible to close the wound and avoid these vessels, they were ligated. After a stormy convalescence with pneumonia, the patient recovered. No pain was felt on the ligation of the vessels, and it is suggested that this was due to the ligatures around the vessel destroying its sensory nerve plexus. The operation was followed by a systolic thrill and murmur, the murmur being ultimately heard over the entire chest. The murmur has persisted and is thought to be due to mitral insufficiency caused by damage to the valve, its chordae tendineae, or papillary muscles as a result of the original stab. Electrocardiography shows changes due to anterior myocardial infarction and occlusion of the coronary vessels.

Olim, C. B., and Hughes, J. D. (1939) *J. thorac. Surg.*, **9**, 99.

HEART DISEASES. ENDOCARDITIS. MALIGNANT

See also B.E.M.P., Vol. VI, p. 297, Cumulative Supplement, Key Nos. 644-646, and Surveys and Abstracts 1939, p. 368.

Erysipelothrix Endocarditis

W. O. Russell and M. I. Lamb reported a case of endocarditis which was proved to be due to the *Erysipelothrix rhusiopathiae*. The presence of the organism was confirmed by complete post-mortem and bacteriological studies. Three probable cases were collected from the literature by the authors, though none of these had been definitely confirmed. This disease is an instance of a chronic form of erysipelo-thrix disease, and is similar in all respects to the endocarditis complicating swine erysipelas.

Russell, W. O., and Lamb, M. I. (1940) *J. Amer. med. Ass.*, **114**, 1045.

Subacute Bacterial Endocarditis

Bacteriology

E. B. Craven *et al.* record 2 cases of subacute bacterial endocarditis caused by *Haemophilus para-influenzae* (Rivers), and review the subject on the basis of 36 cases collected from 1899 to the present time. The morbid changes resemble those of streptococcal endocarditis; acute glomerulo-nephritis is common and meningitis was noted in 5, or 14 per cent, of the 36 cases. The clinical picture, which may be acute, subacute, or chronic, does not differ in any important respect from that of other forms of bacterial endocarditis. *H. para-influenzae* (non-haemolytic) is stated to be the least virulent of this group, but the course of the disease is progressive and uniformly fatal. Treatment by anti-influenzal serum has not been effective.

Treatment

Sulphonamide compounds. According to C. I. Andrews it is difficult to assess the value of chemotherapy in bacterial endocarditis because of the difficulty in diagnosing the condition, the possibility of spontaneous recovery, and the anatomical site of the lesion. Spontaneous recovery is very rare, but undoubtedly occurs. Most of the recorded cases are cases of endocarditis lenta in which the blood-culture has usually been negative. Because those cases which have recovered had a negative blood-culture Andrews concluded that, if the organisms could be killed in the blood-stream, the patient might recover. He reported the case of a man of 68 years in which there was recovery after the use of sulphapyridine. Three courses of the drug were given, 2 orally and the third intramuscularly. In the first course 12 g. were given in 5 days, in the second 6 g. in 2 days, and in the third

2 g. were given intramuscularly. Nausea prevented larger doses, which are more desirable in this condition, being given to this patient.

R. H. Major reported the results of sulphonamide therapy in 7 cases of endocarditis, 3 of which apparently recovered. He had seen no recoveries in a previous 15 consecutive cases treated by other methods. One patient who recovered had received only 15 g. of prontosil and 5 g. of sulphanilamide during 1 month. Another patient who showed no improvement had received a total of 50 g. of prontosil and 95 g. of sulphapyridine. A further patient who recovered had received 144 g. of sulphapyridine, the dosage being 4 g. per day for 36 days. The other patient who apparently recovered had received 6 g. of sulphapyridine daily for 43 days.

J. Heyman treated a case of subacute bacterial endocarditis with sulphanilamide, given in small doses over a period of 6 months, with recovery. The diagnosis was established by means of positive blood-cultures. The average daily dosage of the drug was 20 to 30 grains; after 3 months, the dosage was decreased to between 15 and 20 grains daily. By the end of 6 months the temperature had become stabilized at normal, the pulse rate had fallen to about 90, and chills and sweats had completely disappeared. Eleven months after clinical recovery, blood cultures were sterile.

R. H. A. Swain stated that some cases of subacute endocarditis are benefited by treatment with the sulphonamide compounds whereas others appear to be unaffected by them. He reported 4 cases in which, although the blood might be rendered sterile, the treatment failed. Two of them were quite unaffected by the treatment. The *Strep. viridans* from the 2 unaffected cases were found resistant to the action of sulphonamide compounds *in vitro*. In the 2 other cases the organisms were susceptible. 4,4'-diaminodiphenyl sulphone was found the most potent drug *in vitro*, but it is very much more toxic than sulphapyridine, which is only slightly less active.

H. H. Steele, employing sulphanilamide in 13 cases of subacute bacterial endocarditis, found that the drug had no effect on the general course of the disease. The chief beneficial effect was a fall in the number of bacteria in the blood. In one case there was a fall in the temperature curve coincident with the use of sulphanilamide. In general there were no severe toxic effects. Sulphanilamide did not prolong the life of patients in this series of cases.

W. W. Spink and I. Hughes Crago treated 12 patients suffering from subacute bacterial endocarditis with sulphanilamide. The diagnosis was made upon the history, the presence of an organic cardiac murmur which changed in intensity from time to time, the presence of emboli, and persistent bacteraemia. Twelve of the cases were due to *Strep. viridans* and 1 to *Staph. albus*. The drug made the blood sterile in 6 of the patients, but apparently permanently in only 2 of them. Two of the patients were definitely benefited, but 1 of them died later, 7 months after the apparent cure. The second patient has so far remained in good health for 9 months, but this may prove to be only a remission in the disease. In 4 of the patients the temperature dropped when the drug was given. All the patients had some degree of anaemia and in 1 only did the haemoglobin and red blood-cell count drop as the result of receiving sulphanilamide. In all cases the white blood-cell count was not decreased, and it rose in 2 patients. No correlation between the amount of free sulphanilamide in the blood and its effect upon the bacteraemia could be demonstrated. There were no toxic rashes or cyanosis in this series, but some of the patients suffered from anorexia and vomiting as the result of the drug. Spink and Hughes Crago concluded that sulphanilamide is of doubtful value in the treatment of subacute endocarditis probably because the focus of infection, i.e. the vegetations, is protected from its action.

Fever therapy and sulphanilamide.—I. H. Krusen and R. L. Bennett stated that fever therapy had not been successful in the treatment of subacute bacterial endocarditis due to the streptococcus. Gonococcal cases had received some benefit from it, but this organism is more susceptible to heat. The treatment, however, has been much improved by combining sulphanilamide with it; Krusen and Bennett treated 11 cases of subacute bacterial endocarditis by this means. Only 8 of them received adequate doses of the drug, the dose ranging from 45 to 120 grains. Seven of these patients showed a decrease in the number of colonies on blood-culture. In 2 of the 11 cases the blood-culture became negative for a time. The

treatment was not, however, successful as 10 of the patients died. The remaining one has a positive blood-culture.

Heparin.—M. Friedman *et al.* considered that the infection with *Strep. viridans* in subacute bacterial endocarditis persisted because the rate at which fibrin and platelets are deposited on the heart valve is more rapid than the rate at which the valve can be sterilized. Also the white blood-cells cannot destroy the organism because they cannot reach it through the avascular valve leaflets. The authors therefore suggested that if the formation of fibrin and the deposition of platelets could be prevented by the action of an anticoagulant it might be possible for the heart valve to overcome the infection. A solution containing 30,000 units of heparin in 1 litre of physiological sodium chloride with 5 per cent dextrose was given intravenously for 10 days to a man suffering from subacute bacterial endocarditis. The clotting time of the blood was maintained at 25 to 30 minutes. On the tenth day of treatment the patient died with symptoms suggesting a cerebral haemorrhage. Necropsy showed cerebral haemorrhage following an embolus, endocarditis, infarction of the spleen, and acute glomerular nephritis. In spite of the dangers of the treatment (haemorrhage due to lowering the coagulability of the blood and bacteraemia due to disintegration of a vegetation) the authors think it should have a further trial in this disease, which is invariably fatal in any event. In this case it could not be shown conclusively that heparin prevented the deposition of fibrin and platelets on the heart valves, but the evidence was very suggestive.

I. J. Witts reporting the treatment of a case of subacute bacterial endocarditis with heparin and sulphapyridine lays stress on the importance of the treatment as early in the disease as is possible on account of the occurrence of a haemorrhagic state and renal insufficiency in the later stages, the former increasing the risk and the latter making it difficult for the patient to bear a large amount of fluid given parenterally. The quantity of fluid cannot be less and should not be more than a litre daily if it is to flow regularly through the cannula which should, for a week or 10 days, be tied in with a thread. The patient whose case was reported required about 15 mg. heparin (Roche) an hour to keep the venous coagulation time longer than 1 hour.

Andrews, C. T. (1940) *Brit. med. J.*, **1**, 5.

Craven, L. B., Jr., Posten, M. A. and Orsman, F. S. (1940) *Amer. Heart J.* **19**, 434.

Friedman, M., Hamburger, W. W. and Katz, I. N. (1939) *J. Amer. med. Ass.*, **112**, 1702.

Heyman, J. (1940) *J. Amer. med. Ass.*, **114**, 2373.

Krusin, F. H., and Bennett, R. I. (1940) *Proc. Mayo Clin.*, **15**, 328.

Major, R. H. (1940) *Amer. J. med. Sci.*, **199**, 759.

Rivers, T. M. (1922) *Johns Hopk. Hosp. Bull.*, **33**, 149, 429.

Spink, W. W., and Crago, I. H. (1939) *Arch. intern. Med.*, **64**, 228.

Steele, H. H. (1940) *New Engl. J. Med.*, **222**, 1067.

Swain, R. H. A. (1940) *Brit. med. J.*, **1**, 722.

Witts, I. J. (1940) *Brit. med. J.*, **1**, 484.

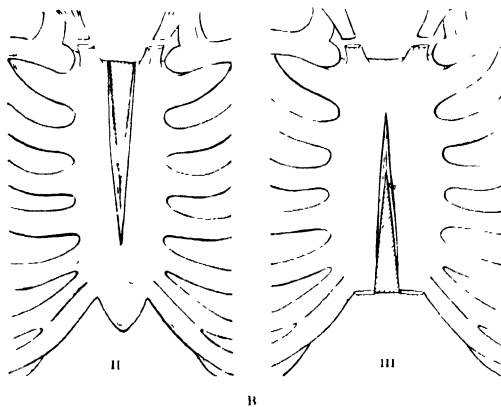
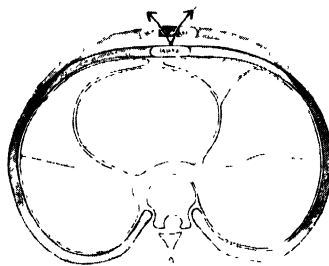
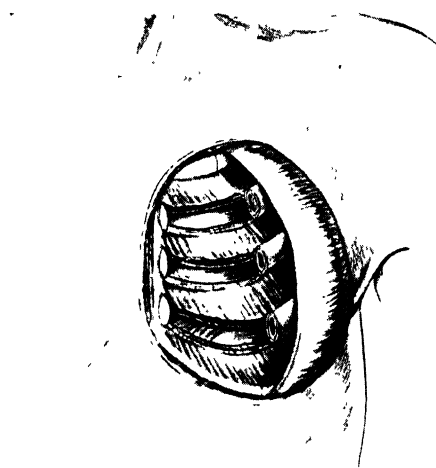
HEART DISEASES—MITRAL VALVE DISEASES

See also B. I. M. P., Vol. VI, p. 309, and Surveys and Abstracts 1939, p. 369.

Mitral Stenosis

B. J. Walsh *et al.* studied 81 young patients with the physical signs of so-called pure mitral stenosis. They found that the evolution of the physical signs before the establishment of this lesion took in most cases 5 to 15 years. It appeared that a relatively mild form of rheumatic fever favoured the development of mitral stenosis. In most patients with this condition the prolonged course of the disease is fundamentally dependent on a benign rheumatic infection.

Walsh, B. J., Bland, E. F. and Jones, T. D. (1940) *Arch. intern. Med.*, **65**, 321.



A. Costal method of cardiac decompression. B. Sternal method of cardiac decompression
(i) diagram of transverse section (ii and iii) anterior aspects (From *Lancet*, 1940)

PLATE II

HEART DISEASES: HEART FAILURE

See also B.L.M.P., Vol. VI, p. 368; Cumulative Supplement, Key No. 659, and Surveys and Abstracts 1939, pp. 20, 59 and 370.

Dropsy*Treatment*

Mercurial diuretics and urea-- M. Winternitz stated that mercurial diuretics are commonly employed to relieve the oedema associated with cardiac failure. They have the disadvantage that the diuresis is often followed by oliguria, and some diuretic, as well as the restriction of fluids, has to be given between the injections to maintain the diuresis. Theobromine compounds are useless for this purpose. Winternitz used urea instead. Twenty-four to 48 hours after the mercurial injection 20 to 40 gr. of urea were given in strong, unsweetened coffee daily. This treatment was invariably successful, diuresis appearing on the first or second day. There were no unpleasant reactions. Three successful cases were reported in detail.

Winternitz, M. (1940) *Lancet*, **1**, 879

Blood Viscosity*Treatment*

Calcium gluconate A. S. Rogen investigated the blood-viscosity of 6 normal persons and 20 patients suffering from heart failure, before and after 10 c.c. of a 10 per cent solution of calcium gluconate had been given intravenously. He previously found that in those with heart failure but no oedema the blood-viscosity tends to be raised. When oedema was present and there was little venous congestion, the viscosity was low. The calcium did not affect the viscosity in normal individuals, but reduced it in those who had venous congestion without oedema. If oedema were present the viscosity was sometimes lowered, sometimes raised, and sometimes unaffected. The drug acts as a tonic to the heart in patients suffering from heart failure, and, by decreasing the viscosity of the blood, renders the heart's action more efficient.

Rogen, A. S. (1940) *Lancet*, **1**, 780

Cardiac Compression*Treatment*

I. O'Shaughnessy pointed out that the mediastinum is such a small space that the enlargement of benign tumours or neighbouring structures may cause death by pressing upon vital structures within it. Among such conditions is hypertrophy of the heart, which the elastic chest wall of the child can accommodate, but which in adults may cause death from pressure. He reported such a case in a woman of 21 years. The heart may be pressed upon by such conditions as a large pleural exudate. This leads to cardiac dysfunction, notably impairment of venous return. A rigid chest wall with a hypertrophied heart produces the same result. O'Shaughnessy described 2 operations to relieve this rigidity and decompress the heart. Part of the ribs concerned may be removed or a median sternotomy may be done. The hypertrophied heart may be allowed to expand by incising the tight pericardium and thus relieving the pressure. There is some difference of opinion as to the results of this operation, but O'Shaughnessy has performed it with some benefit. Some observers regard the intact pericardium as useful in cases of heart disease as it prevents, or at any rate delays, dilatation and cardiac failure. (See Plate II.)

O'Shaughnessy, L. (1940) *Lancet*, **1**, 61

Treatment*Action of Digitalis*

H. Gold and M. Cattell had previously shown that digitalis glucosides increased the force of contraction of failing mammalian cardiac muscle by direct action on the muscle. A further series of experiments produced evidence that the heart muscle is not overdistended in clinical heart failure, and that dilatation of the heart is not usually an unfavourable phenomenon, but an adaptive mechanism by which the

failing heart maintains its optimal capacity for work. The high venous pressure in heart failure is not generally a cause but a result of heart failure. There is no sufficient reason for the belief that venous congestion of the kind seen in clinical heart failure embarrasses the heart's contraction. Rapid heart rate in sinus arrhythmia and auricular fibrillation is usually not a cause but a result of heart failure. The effect of digitalis in abolishing heart failure is not mediated through any effect in the average case, through action on the splanchnic circulation (constriction of hepatic veins), or through action on cardiac tone. In therapeutic concentrations digitalis exerts no direct action on the heart muscle, which, without primary change in the diastolic length of the muscle, increases the tension which the muscle can develop during systole.

Digitalis

W. Evans describes a clinical assay of 6 preparations of digitalis: digitalis leaf, tincture of digitalis, digoxin, digitaline (Nativelle), digitaline (Allen and Hanbury's) and digifoline, and of 3 other drugs with a digitalis-like action, folinerin, strophanthin and ouabaine; cardiazol and coramine were used as controls. Eighteen patients (12 females, 6 males, with an average age of 48 years) with auricular fibrillation of rheumatic origin, as shown by the presence of mitral stenosis, and cardiac failure were all treated as out-patients and seen every fortnight; they were each given a fortnight's administration of each of the digitalis and other preparations. The following were the results: efficient digitalization was always induced and maintained by powdered digitalis leaf, digitaline (Nativelle), digifoline, digoxin, tincture of digitalis, and digitaline (Allen and Hanbury's) mentioned in the order of their therapeutic activity in customary doses and from a practical standpoint. Powdered digitalis leaf was the most successful, and was also one of the cheaper preparations. Digitaline (Nativelle) in a dose of $\frac{1}{16}$ grain (pink granule) showed greater digitalis effect than digitaline (Allen and Hanbury's) in a dose of $\frac{1}{16}$ grain (white granule). Digitaline (Nativelle) in a dose of $\frac{1}{16}$ grain (white granule) proved too potent for continuous use. Folinerin, ouabaine and strophanthin (orally) failed to produce adequate digitalization, and their routine use in heart failure appeared in every patient when either cardiazol (metrazol), with a formula allied to camphor or coramine was prescribed without digitalis. The optimal dose of digitalis could not be predicted with any accuracy, and it had to be sought by trial and error, thus implying a therapeutic study in every patient.

Convallan

R. H. Major and L. H. Leger discussed the results obtained from the use of convallan, an extract obtained by treating an aqueous solution of *Convallaria majalis* with colloidal iron hydroxide and concentrating the filtrate to a powder. This extract has been found to consist of 20 per cent convallatoxin and 80 per cent 'convallamarin complex'. Physiological assays have shown that convallan contains 4,000 to 8,000 frog doses per gram. Therapeutic activity of convallan has been found to be between that of digitalin and strophanthin. Buttner (1937) found that the minimal effective dose of convallan was 3,000 frog units, that the maximal dose was 20,000 units, and that doses of 12,000 units could be given with safety. Buttner also found that convallan had little, if any, cumulative action, and could be given safely before or after digitalization. In large doses its action was essentially the same as that of digitalis or strophanthin, but small doses produced a remarkable diuretic effect without causing heart-block, or increasing the degree of an already existing block. Major and Leger therefore employed the drug in patients with heart failure associated with varying degrees of heart-block. The dosage employed was determined by the effects obtained in each patient, varying from 2,000 to 3,000 units daily. In many cases great benefit was obtained in cases of heart-block or bundle-branch block in which the administration of digitalis was inadvisable. Rapid loss of anasarca and dyspnoea, and slowing of pulse rate was a common effect. In some cases improvement in auriculo-ventricular conduction occurred.

Surgical Measures

Thyroidectomy—H. Siedek discusses the question of thyroidectomy for cardiac and vascular diseases.

Complete thyroidectomy influences the heart by diminishing the tone of the autonomic nervous system, and also impedes the process of inflammation in the heart and blood vessels, but myxoedema is always a possible sequel. Hyperthyroidism is more suitable for the operation than 'thyroid-normal' persons. Severe vascular disease, especially of the cerebral blood vessels, and myocarditis contraindicate operation. Patients with angina pectoris will be improved by removal of the thyroid if the heart is still powerful. Even in cardiac failure attacks of cardiac asthma will disappear after thyroidectomy.

In angina pectoris with coronary obstruction, however slight, thyroidectomy is contra-indicated.

Büttner, — (1936) *Munch. med. Wschr.*, **83**, 387.

Evans, W. (1940) *Brit. Heart J.*, **2**, 51.

Gold, H., and Cattell, M. (1940) *Arch. intern. Med.*, **65**, 263.

Major, R. H., and Eger, I. H. (1939) *Am. Heart J.*, **18**, 444.

Siedek, H. (1939) *Dtsch. med. Wschr.*, **65**, 1225.

HEAT-STROKE AND HEAT-EXHAUSTION

See also B.E.M.P., Vol. VI, p. 396, and Cumulative Supplement, Key No. 661.

Pathology and Morbid Anatomy

Cardiac Changes

G. Wilson describes the morbid changes in 4 fatal cases of heat-stroke. One patient was a victim of sunstroke and the other 3 died after artificially induced fever. The cardiac lesions were very like those in deaths from electricity or lightning. Extensive subendocardial haemorrhages in the left ventricle, and subcutaneous, intramuscular, and intracerebral petechiae were also found in some cases. Cerebral oedema was also seen. The condition is characterized by a persistent rise of temperature, as high as 110° F. in one case, later followed by unconsciousness.

Wilson, G. (1940) *J. Amer. med. Ass.*, **114**, 557.

HEREDITY AND CONSTITUTION

See also B.E.M.P., Vol. VI, p. 452.

Constitution

Relation between Kretschmer's Types and Menstrual History

F. Wallou reports his observations on the relation between the constitutional types of women and their reaction to the menstrual cycle. Over 2,000 patients were examined and classified as either leptosome-asthenic (the tall, slim woman) or pyknic (the small 'round-shaped' woman). It was found that the pyknic type has an inherent hereditary factor for an early onset of menstruation, whereas the asthenic type starts menstruation later. The asthenic type menstruates more freely and for a longer time than the pyknic woman and suffers less from anomalies of the period other than dysmenorrhoea which is predominantly found in this type, the asthenic type shows less predisposition to develop malignant growth than the pyknic woman, though having a far greater predisposition for retroflexion. The author emphasizes the interest of similar studies in the prophylaxis of menstrual disturbances.

Wallou, F. (1939) *Zbl. Gynaek.*, **19**, 1830.

HERNIA

See also B.E.M.P., Vol. VI, p. 470, Cumulative Supplement, Key Nos. 672-687; Surveys and Abstracts 1939, p. 372; and p. 12 of this volume.

External Abdominal Hernia

Aetiology

Relation to trauma—J. J. Moorhead analyses his operative findings in 1,376 herniotomies in which trauma was the alleged factor causing the hernia, and concludes that hernia is never caused by injury, the formation of the sac being

always antecedent, but it may be *aggravated* by injury, if the source and symptoms are adequate. The operative findings generally denote an earlier process, as shown by adhesions, extrasaccular and intrasaccular. Pathological examination of the sac demonstrates chronic peritonitis and fibrosis. Hernia is a chronic progressive disease, a ptosis and a diverticulum, and only rarely an acute surgical factor. A large proportion of adults have hernia without their knowledge and, like osteomyelitis, hernia is subject to periods of accession and remission.

Clinical Picture

Strangulation in the aged—O. T. Clagett reports operation on cases of acute strangulation in 8 patients, aged 70 or more years, the oldest being 86 years of age, with 1 death, in a man aged 70, whose hernia had been strangulated for 48 hours. Two were women, both with femoral hernia, and 6 men, 5 with inguinal and 1 with femoral hernia. Local anaesthesia, in some cases supplemented by intravenous pentothal sodium, was employed. The medical profession were still inclined to overrate the danger of operation in advanced life, it was not the actual age, so much as the physiological and pathological condition of the tissue that counted, and the survival of the individual to the age of 70 or 80 was presumptive evidence that his body is better able than the average to withstand the strains of life. Surgical treatment of the aged was becoming increasingly important, because, as Brooks pointed out, Americans now enjoy a longer expectancy of life, from 39 years in 1850 to 59 years in 1931. Preventive surgery, such as herniotomy before an emergency arises, should be more widely recognized and acted upon. In the discussion after this paper, J. M. Waugh pointed out that the repair of a strangulated hernia carried with it 30 times the risk of operation on an uncomplicated inguinal hernia. Two important factors in operations on old people were the use of local anaesthesia as described above, and early active movement after operation; practically all the patients reported were out of bed in a chair on the first or second day after operation.

Brooks, B. (1937) *Ann. Surg.*, **105**, 481.

Clagett, O. T. (1939) *Proc. Mayo Clin.*, **14**, 797.

Moorhead, J. J. (1940) *Am. J. Surg.*, **47**, 312.

Waugh, J. M. (1939) *Proc. Mayo Clin.*, **14**, 799.

Treatment

Fascial Suture

W. Gray reports on 54 inguinal hernias in 50 patients treated by fascial suture, 4 of these 50 patients having bilateral lesions. Twenty-nine were cases of oblique hernia, 10 were direct, and in 11 the type was not stated in the records. The remaining 4 cases had already recurred after operation elsewhere. The average period which had elapsed between operation and the date of investigation was 3 years. The main points of the technique employed during the operation in this series were that the sac was not cut away after being separated, but was stitched and pulled up under the internal oblique muscle after Macewen's method. A fascial suture was obtained from the aponeurosis of the external oblique and was inserted *in front* of the cord. The conjoined tendon was not utilized, since it is often poorly developed and has little strength; instead the fascial stitches passed from the inguinal (Poupart's) ligament to the edge of the sheath of the rectus abdominis *without tension*. It was found that when a hernia did recur, as it did in 4 cases (7.4 per cent) in this series, it ran alongside of the cord and appeared at the side of the original ring, the technique was therefore altered by the insertion of the fascial suture *behind* the cord.

J. L. McClosky and J. A. Lehman also stated that living fascia is superior to all other suture materials in the repair of large herniae. They also found that the percentage of recurrences is definitely lowered; in a series of 82 cases, there were only 4.

Injection Therapy

End results—H. K. Sowles and W. M. Shedden report that among 109 cases of inguinal hernia treated by injection and followed up, 32 (29 per cent) had recurrences. The longest period during which any patient remained cured was 42 months, the average period being 14 months. The advantages of injection treatment are that it is safe, there are no serious complications and even minor complications, such as pain, puncture of a blood vessel, induration of the cord and peritoneal irritation,

are not serious, and the patient remains ambulatory during treatment. The chief disadvantages are that it is prolonged, and that the recurrence rate is higher than would be expected from expert surgery. The most suitable patients are those with good muscular development, not obese, and with an indirect inguinal hernia of small or moderate size.

G. Marcucci discussed the present outlook in Italy on the injection treatment of herniae. This method is much used and therefore the author undertook a critical investigation to establish its exact value. Many practitioners give only 1 injection, this is always followed by recurrence of the hernia, even if it is at all benefited. McDonald's solution of alcohol, phenol, and oil of thuja was found to be the most useful sclerosing agent and the reaction set up thereby is a polymorphonuclear exudation with stimulation of connective tissue proliferation, which must be directed by the technique of injection medially to the spermatic cord. If the injected sclerosing agent reaches the vas, complications arise which detract from the initial success, this leads the author to warn against the indiscriminate use of this method. Gangrene of the testis, and intraperitoneal complications such as obstruction and formation of adhesions were among the many complications recorded.

Surgery

End results—C. C. Burton and R. L. Ramos give a statistical survey of 130 recurrent hernias which were again treated by operation. Of these, 101 patients were followed up for a maximal period of 54 months, and 76 per cent were re-examined by medical practitioners. So far there had been 14 recurrences, or 13.6 per cent of the total followed up. With regard to the causes of failure, the most striking finding concerning the sacs was the marked preponderance of the direct type in 54.7 per cent, bilocular in 20.6 per cent, and diverticular in 13.8 per cent of the recurrent hernias. The importance of the integrity of the fascia transversalis was emphasized.

Herniotomy in Old Age

A case of herniotomy for double inguinal hernia in a man, aged 93, was reported in 1932 by Grey Turner who in 1940 pointed out that, though strangulation demands operation whatever life's span, the wisdom of a radical operation, in exceptional circumstances, was doubtful in extreme old age. L. W. Innes reported that a man, aged 96, survived operation for a strangulated inguinal hernia in 1925 until he was probably a centenarian. R. Fawcitt recorded the case of a woman, aged 91, who was operated upon for a strangulated femoral hernia and died 6 months later from cerebral haemorrhage. J. L. R. Edwards operated successfully on a man, aged 92, with a strangulated inguinal hernia.

J. A. Ross and A. Fraser report a successful operation for a strangulated right inguinal hernia in a man aged 93 years and from a survey of a number of published collections of cases did not find any comparable case. Paul Berger among 9,946 cases of hernia noted one patient of more than 90 years of age with a bilateral inguinal hernia, but did not state whether or not he was operated upon.

- Berger, P. (1896) *Dix mille observations de hernies*, Paris.
- Burton, C. C., and Ramos, R. L. (1940) *Surg. Gynec. Obstet.*, **70**, 969.
- Edwards, J. L. R. (1940) *Brit. med. J.*, **1**, 417.
- Fawcitt, R. (1940) *Brit. med. J.*, **1**, 417.
- Gray, W. (1940) *Brit. med. J.*, **1**, 568.
- Innes, L. W. (1940) *Brit. med. J.*, **1**, 507.
- McCloskey, J. F., and Lehman, J. A. (1940) *Ann. Surg.*, **111**, 610.
- Marcucci, G. (1939) *Arch. ital. Chir.*, **56**, 339.
- Ross, J. A., and Fraser, A. (1940) *Brit. med. J.*, **1**, 256.
- Sowles, H. K., and Shedden, W. M. (1940) *New Engl. J. Med.*, **222**, 753.
- Turner, G. G. (1932) *Brit. med. J.*, **1**, 410.
- (1940) *ibid.*, **1**, 332.

HERPES

See also B. E. M. P., Vol. VI, p. 513, and Surveys and Abstracts 1939, p. 373.

Recurrent Traumatic Herpes

G. M. Indlay and F. O. MacCallum describe a case of recurrent traumatic herpes,

of which only 4 similar cases have been reported previously. It has been shown that infection with the virus of herpes occurs, at any rate in the poor, in the first years of life. In infants it causes epidemic stomatitis. Once acquired, the virus remains latent, giving rise to recurrent attacks of labial herpes. In recurrent traumatic herpes, a traumatic skin lesion is followed at intervals for years by a recurrent herpetic eruption, often associated with neuralgia of the local nerve supply. The author's patient, a child, fell down and grazed her hand when 20 months old. At intervals for the past 5 years she has been liable to typical herpetic eruptions at the site of the lesion. The virus isolated from these lesions was highly encephalitogenic to mice. The most probable source of the virus in these traumatic cases is the saliva. Attempts to isolate the virus from the epidermal cells have failed. It seems more likely that the virus remains latent in the ganglion cells of the nerve roots, though this is by no means certain.

Findlay, G. M. and MacCallum, F. O. (1940) *Lancet*, **1**, 259

HISTOPLASMOSIS

See also B I M P., Vol. VI, p. 520.

Clinical Picture

A I. Amolsch and J. H. Wax report the tenth published case of histoplasmosis, in a female infant, who had a cough soon after birth, and 9 weeks later became pale, the spleen was enlarged, and the temperature rose. The blood showed 50 per cent of haemoglobin, a low red-cell count, and a persistent leucopenia. Splenic anaemia was diagnosed and the spleen was removed. The blood picture then definitely improved but the fever, weakness, and abdominal enlargement persisted. The infant died 3 weeks after splenectomy at the age of 8 months. Necropsy was refused, but examination of the spleen showed great proliferation of the reticulo-endothelial system. There were also many large macrophages containing up to 25 parasites. Re-examination of the blood smears taken during life showed phagocytosis of the parasites in large mononuclear cells and occasionally in neutrophil polymorphs. The authors stated that the characteristic feature of the condition is the clusters of phagocytosed yeast-like fungi in the reticulo-endothelial cells. As 6 of the reported cases presented respiratory symptoms, that tract might be the portal of entry, but in other cases the gastro-intestinal tract has been more prominently affected.

Amolsch, A. I., and Wax, J. H. (1939) *Amer. J. Path.*, **15**, 477

HODGKIN'S DISEASE

See also B I M P., Vol. VI, p. 523, Cumulative Supplement, Key No. 691; and Surveys and Abstracts 1939, p. 375

Aetiology, Clinical Picture and Prognosis

From an analysis of 212 cases of Hodgkin's disease, L. B. Goldman draws the following conclusions. The disease is most common in men between 20 and 40 years of age and its occurrence in girls under 15 years of age is rare. No apparent predisposing factors were found in any case. Enlargement of the lymph nodes was the presenting sign in 79 per cent of the cases. In 9 patients pruritus occurred from 3 weeks to 4 years before the enlargement of the glands; in early stages lymphadenopathy was more often unilateral than bilateral, and splenomegaly was infrequent, though generally present in advanced cases. There is not any constant pathognomonic X-ray appearance, but in 19 cases there were nodules throughout the lungs. In 80 cases the skin was involved, the manifestations varying from pruritus to multiple nodules, and occasionally generalized exfoliative dermatitis. In 14 cases there were radiological changes, generally osteolytic, of the bones. There were 10 cases of diplegia, 8 at the dorsal and 2 at the lumbar level. The most constant blood change is a fall in the lymphocyte count. In most cases a continuous low-grade fever is present, but the Pel-Ebstein type is uncommon. In advanced cases a striking feature is the marked elevation of the pulse rate, out of proportion to the rise in temperature. The average duration of life after the onset of symptoms of the 123 patients who died under observation was 32.06 months. The average

duration of life after the institution of therapy was 23.8 months. Eleven patients lived 5 years or more after irradiation. The disease varied greatly in virulence, clinical course, and response to treatment.

Isolated Gastric Lesions

C. H. Avent reported the rare condition of Hodgkin's disease confined to the stomach in a woman aged 63. She complained of indigestion for 6 months—epigastric fullness and burning pain without any relation to food, and more recently of loss of weight, constipation, nausea and vomiting, sometimes 'coffee grounds', and tarry stools. A firm, tender, freely movable mass was palpable in the mid-epigastrium. There was some degree of anaemia and the faeces and vomit contained blood. X-ray examination showed a pre-pyloric filling-defect and a diagnosis of gastric carcinoma was made. Laparotomy showed a freely movable gastric mass without enlargement of the liver, and mesenteric and retroperitoneal glands. Partial gastrectomy was performed and the patient died of broncho-pneumonia 4 days later. Permission for necropsy was refused but examination of the part removed at operation showed lymphogranulomatosis of the stomach with ulceration. From a review of 9 reported cases of Hodgkin's disease of the stomach, the author concluded that the prognosis must be guarded, even after the gastric lesion has been removed, as subsequent lesions have appeared elsewhere and that diagnosis is almost impossible without microscopic examination of the lesion.

Hyperchromic Macrocytic Anaemia

S. R. Townsend and A. L. Braunstein report a case of Hodgkin's disease with hyperchromic macrocytic anaemia in a woman, aged 59 years, and they could refer only to the 3 somewhat similar cases reported by I. S. P. Davidson in 1932, the anaemia of Hodgkin's disease being usually of the secondary type. Clinically, the patient did not suggest Addisonian anaemia, but the blood examination did. There were, however, some reasons for doubt: gastric analysis showed 34 degrees of hydrochloric acid after histamine, and there was not any evidence of haemolytic anaemia by laboratory tests, and at the necropsy there was not any increase of iron pigment in the liver, kidneys, spleen, or bone-marrow, nor any hyperplasia of the red bone-marrow. The anaemia was ascribed to diminution in the amount of functionally active bone-marrow, caused by replacement: the vertebrae showed lymphadenomatous infiltration whereas in the bone-marrow of the right femur the fat was occupied by numerous haemorrhages, a few patches of myeloid hyperplasia, but not by any lymphadenomatous growth.

Avent, C. H. (1939) *Arch. Surg., Chicago*, **39**, 423.

Davidson, I. S. P. (1932) *Quart. J. Med.*, N.S. **1**, 543.

Goldman, L. B. (1940) *J. Amer. med. Ass.*, **114**, 1611.

Townsend, S. R., and Braunstein, A. L. (1939) *Canad. med. Ass. J.*, **41**, 254.

Diagnosis and Differential Diagnosis

Giant Follicular Lymphadenopathy

Under the above title C. Powell records 2 cases of the condition previously described by Brill, Baehr, and Rosenthal, as splenomegalia lymphatica hyperplastica, which D. Symmers in 1938 divided into 2 groups: (i) in which the enlarged follicles remain as such for months or years, or the lymph nodes become small and disappear for a time, only to recur, or they may break down and discharge a thin fluid, then heal and disappear; (ii) in which the condition becomes transformed into (a) polymorphous celled sarcoma, (b) Hodgkin's disease, or (c) lymphoid leukaemia. One of Powell's cases had a history of more than 20 years and remained quiescent all the time, and so belonged to the first, the benign, group in which the morphology of the lesion does not change. The other patient may have been the subject of the disease for 4 or 5 years and may also be an example of the benign group. The prognosis is difficult: so long as the glands remain radioactive, the disease may be controlled. Deep X-ray treatment is the only effective means, and, it is said, should be repeated at intervals of 3 months.

Brill, N. L., Baehr, G., and Rosenthal, N. (1925) *J. Amer. med. Ass.*, **84**, 668.

Powell, C. (1940) *Canad. med. Ass. J.*, **42**, 372.

Symmers, D. (1938) *Arch. Path.*, **26**, 603.

Treatment

X-ray Therapy

R. Gilbert summarizes his results from the radiological treatment of Hodgkin's disease. He claims that radiotherapy, even if it cannot cure, can prolong life and relieve the symptoms. With regard to acquired radio-resistance, the author claims that it is due to wrong treatment, i.e., too small doses, or repeated irradiations with short waves. The aim of radiotherapy should be to obtain remission of symptoms as completely and for as long as possible. Excellent results have been obtained with radium, but, in view of the large surfaces that have to be irradiated and of the doses to be administered, the author prefers X-rays. Irradiation of the whole body is dangerous and unnecessary, localized irradiation being the treatment of choice. The fields should be determined after clinical observation and in the light of anatomical knowledge.

The author defines the optimal dose as the smallest dose which will destroy the granulomatous tissue without affecting the organism. That dose varies greatly according to the patient. He uses fractionated, fortnightly, localized irradiations, especially to those areas which are clinically threatening. The dose at one sitting is usually 20 r, it may be much less if the general state of the patient is bad. The minimal total deep dose per part is 500 r for a radiosensitive patient. It should be augmented to individual requirements. X-ray therapy should not be repeated before the appearance of a relapse; repetition is not only superfluous but dangerous.

X-ray baths. W. M. Levitt employed a method of X-ray bath irradiation in 202 cases of lymphadenoma and radiosensitive malignant disease, over a 10-year period. The object of the method was to secure maximal dose concentration with safety, and all parts of the body not to be irradiated were protected. High-voltage X-rays were employed: 180 kv in the earlier cases and 200 kv in the late. The filter was 0.5 mm. of copper with 180 kv, and Thoraeus with 200 kv. Long focal-skin-distances were used: 60 to 140 cm., according to the size of the field. Irradiation was always effected with 4 oblique fields, the central rays of which were directed so as to meet at the central point of the cross-section, making equal angles at this point. Trunk baths consisted of irradiation of the whole trunk from the mandible to the groins. In the thoracic baths, the chest, neck, and axilla were treated, and in the abdominal bath the area exposed was from the ensiform cartilage to the inguinal glands. Of 103 cases of lymphadenoma, of a possible 7, only 2 lived for 7 years or over, and of a possible 61, 16 (26 per cent) lived for 5 years and over, and of these 9 (15 per cent) are still alive. In 12 cases of lymphosarcoma, 2 of a possible 7 survived 5 years and over, and are still alive. The disadvantage of the method is that the patient has to remain away from work for about 3 months.

Gilbert, R. (1939) *J. belge Radiol.* **28**, 327.

Levitt, W. M. (1940) *Lancet*, **1**, 212.

HYDROCEPHALUS

See also B.I.M.P., Vol. VI, p. 566

Hydrocephalus following Subarachnoid Haemorrhage

H. R. Merwarth and I. S. Freiman record a case of a female infant, one of twins born in a breech presentation, without any evidence of intracranial lesion until the age of 5 weeks when projectile vomiting occurred, and the head was turned to the right. Lumbar puncture gave exit to blood-stained cerebrospinal fluid with xanthochromia. Subarachnoid haemorrhage was diagnosed. The Wassermann reaction was negative in the infant and the parents. The patient was discharged on the tenth day; but the head progressively increased in size in spite of repeated lumbar puncture, and hydrocephalus was diagnosed. Readmitted when 3½ months old, the infant died 3 days later. At the necropsy all the cerebral ventricles and the Sylvian aqueduct were dilated, and the ventricles contained fresh blood, which came from a congenital angioma in the left optic thalamus. There was evidence of past haemorrhage in the presence of pigmented phagocytes. The pia-arachnoid was widely thickened, ascribed to organization of extravasated blood, and regarded as

the obstructive cause of the hydrocephalus. Treatment of subarachnoid haemorrhage by repeated lumbar puncture is recommended both for its immediate therapeutic effect and as a preventive of the potential sequel of hydrocephalus.

Meiwarth, H. R., and Freiman, I. S. (1939) *Brooklyn Hosp. J.*, **1**, 149.

Otitic Hydrocephalus

N. Asherson reported 7 cases of otitic hydrocephalus, and 2 cases which simulated it. He divided the condition into 2 types, those having no localizing signs and those with encephalitis producing localizing signs and changes in the cerebrospinal fluid. The first is the classical type. Acute internal hydrocephalus follows infection of the ear, but recovers spontaneously. It usually occurs in children or young adults. Headache, vomiting, and papilloedema occur with raised cerebrospinal fluid pressure. The papilloedema appears early and is the last sign to disappear. The patient is usually well between the attacks of headache and vomiting. Recovery takes place after repeated lumbar puncture, in from 2 to 6 weeks. Asherson reported 4 cases of this type and 1 other case in which papilloedema was absent.

In the second type an encephalitis of the temporal lobe occurs producing localizing signs simulating an otitic temporal lobe abscess. It most often follows thrombosis of the lateral sinus when the internal jugular vein has been ligated. It is the blocking in the intracranial venous system rather than infection which produces this type. The treatment is repeated lumbar puncture and the prognosis is good. He reported a case of this kind and another similar one, but streptococcal due to a leptomeningitis were present in the cerebrospinal fluid.

Similar symptoms to those of otitic hydrocephalus have been encountered during the symptomless period of lobar pneumonia. Asherson reported the cases of 2 children, also suffering from acute otitis media, in which this condition was found. It may be differentiated from otitic hydrocephalus by an X-ray examination of the chest and by a blood count, which shows the great rise in polymorphonuclear cells characteristic of pneumonia.

Asherson, N. (1939) *J. Laryng.*, **54**, 319.

ICHTHYOSIS

See also B.F.M.P., Vol. VII, p. 52, and Surveys and Abstracts 1939, p. 379.

Keratosi Verrucosa

I. Keimig described 2 cases of keratosi verrucosa, one of which was lichen obtusus and the other, in his opinion, neurodermatitis circumscripta follicularis. The author disagreed with the suggestion that keratosi verrucosa is a form of primary keratosis, on the grounds that in most of the reported cases the patient was over 40 years old, that itching is generally severe, and that there is no evidence of heredity. He held that keratosi verrucosa is not a single clinical entity, but a manifestation of lichen planus, eczema, neurodermatitis, or urticaria perstans.

Keimig, L. (1939) *Derm. Wschr.*, **108**, 729.

IMPETIGO

See also B.F.M.P., Vol. VII, p. 81; Cumulative Supplement, Key Nos. 734 and 735, and Surveys and Abstracts 1939, p. 381.

Impetigo Contagiosa

Treatment

Calomel ointment. T. Cornbleet *et al.* reported the use of colloridal calomel ointment in various dermatoses; 130 cases of impetigo contagiosa were successfully treated with it. The eruption cleared on an average in one-third to one-half the time required by ointments of ammoniated mercury. The ointment was not toxic.

and was clearly in use. It also improved leg ulcers with secondary pyogenic infection, and some forms of seborrheic eczema and early cases of psoriasis. In other cases such as furunculosis, lichen planus, and lupus vulgaris no benefit was derived from the ointment.

Rubber impregnated with 8-hydroxyquinoline M. Seldowitz treated 38 children suffering from impetigo contagiosa with rubber containing 8-hydroxyquinoline. This compound has been found to be bacteriostatic, especially to staphylococci. Eleven of the children had the bullous type of lesion, and the rest the confluent crusted type. In applying the compound care was taken not to disturb the crusts mechanically. It was applied over a thin layer of gauze and was held in place by adhesive bandages which were changed every 2 to 4 days. In only 3 cases was this treatment unsatisfactory. In the others the crusts disappeared on an average in 3 days and the skin was normal on an average in 8 days. In 2 of the unsuccessful cases the impetigo was complicated by the presence of eczema, and in the third the condition recurred repeatedly usually after abrasion of the skin.

Cornbleet, T., Slepian, A. H., and Ebert, M. H. (1939) *J. Amer. med. Ass.*, **113**, 1804.

Seldowitz, M. (1940) *Amer. J. Dis. Child.*, **59**, 67.

INFANT FEEDING: THE FEEDING OF NORMAL INFANTS AND CHILDREN

See also B.L.M.P., Vol. VII, p. 136; Cumulative Supplement, Key Nos. 749-753, and Surveys and Abstracts 1939, p. 381.

Breast Feeding

Antrachitic Value of Human Milks

J. C. Drummond *et al.* studied the antrachitic value of human milks. The mean value of 16 samples taken during the winter months was 5.9 I.U. vitamin D per 100 c.cm.; for 10 summer samples it was 6.2 I.U. Large doses of vitamin D given to mothers during pregnancy did not produce proportional increases in the vitamin D content of the milk. Probably the minimal safe intake per day of vitamin D in the pregnant or lactating woman is 200 to 300 I.U. Human milk contains about 30 mg. per cent of calcium and 15 mg. per cent of phosphorus, compared with cow's milk which contains about 130 mg. per cent of calcium and 85 mg. per cent of phosphorus. It is possible that infants have a reserve store of calcium at birth to make up for the deficiency in the maternal milk.

Effect of Prolactin in Nursing Women

M. Kenny and I. King studied the effect of prolactin on lactation in nursing women. Forty-three women deficient in milk secretion were treated, some with prolactin from ox pituitaries and others with prolactin from sheep's pituitaries. In 75 per cent of the women the results were satisfactory and the secretion of milk became normal. There were no adverse local or general effects from treatment with the hormone. A few of the cases showed only a temporary moderate increase in secretion, and in 19 per cent of the cases there was little or none at all. The quality of the milk in this series was exactly the same as that taken from normal untreated women. Prolactin was given in the early stages of the period of lactation when clinical experience or past history indicated that the patient would probably not have sufficient milk. In the later weeks deficiency or decrease in lactation was treated. A total dosage of 15 c.cm. (900 Riddle crop-gland units) of prolactin was given, over a period of 5 days. On each of the first and second days 5 c.cm. were injected intramuscularly, on each of the third and fourth days 2 c.cm. were given; and on the fifth day 1 c.cm. was given.

Drummond, J. C., Gray, C. H., and Richardson, N. E. G. (1939) *Brit. med. J.*, **2**, 757.

Kenny, M., and King, E. (1939) *Lancet*, **2**, 828.

INJURIES

See also Surveys and Abstracts 1939, p. 383.

Wounds

Sources of Haemolytic Streptococcal Infection

R. Hare discusses the sources of haemolytic streptococcal infection of wounds in war and civil life. Only those of group A are now considered to be seriously pathogenic to man. Infections, of which the patient is not aware, may exist in the neighbourhood of the wound. Thus haemolytic streptococci of group A may occur in the tonsils or be present during a common cold. The patient or his attendants may carry the organism on their skin, in the nasopharynx or in the faeces. Infected air, soil, clothing, instruments and dressings, and food are other possible sources of infection. During the last war the infection was usually established by the time the patient reached the casualty clearing station and during this time the patient had been in contact with approximately 333 people. Since 7 per cent of people carry the organism in the nasopharynx it is reasonable to suppose that they were the source of the majority of the infections. At base hospitals an infection from other wounds in the vicinity has been described. It is probable that civilian casualties during air-raids will become infected in the same way. It is suggested that to prevent these infections all attendants should wear masks and, if possible, sterile rubber gloves. In the absence of the latter the hands should be protected with some antiseptic. All infected cases should be carefully segregated from those surgically 'clear'.

Hare, R. (1940) *Lancet*, **1**, 109

Penetrating Wounds of Abdomen

A. H. Storck reported on 46 cases of penetrating wounds of the abdomen, 35 of which were gunshot wounds and 11 stab wounds. The mortality of the gunshot wounds was 40 per cent, and of the stab wounds 27.2 per cent. Symptoms are often indefinite, and pain is frequently slight or absent. Tenderness and rigidity are not constantly present. Time-consuming procedures such as intestinal resection should be avoided whenever possible. Silk or cotton sutures and ligatures are superior to catgut for the repair of hollow viscera and for the closure of the abdominal wall.

Storck, A. H. (1940) *Ann. Surg.*, **111**, 775

Treatment

Control of Arterial Haemorrhage

New type of tourniquet.—L. D. Callander described an improved type of tourniquet. This is similar in pattern to Sanways' anchor tourniquet, but the anchor is fitted with a corkscrew handle so that it can be firmly held and the free end can easily be inserted under the wing of the anchor. Very soft rubber tubing is used to minimize the danger of injury to the tissues and to ensure that the tourniquet lies flat.

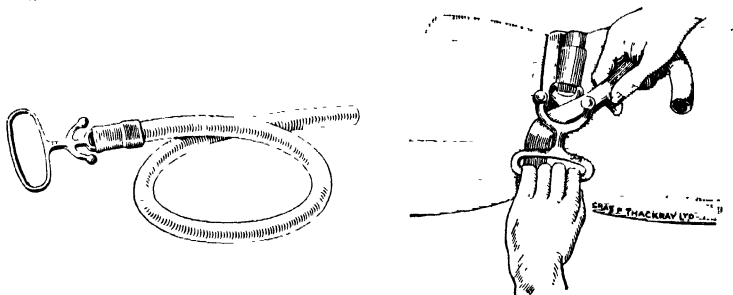


FIG. 9. —Improved type of tourniquet. (From *Lancet*, 1940)

Intramuscular Injection of Fluids

B. R. Billimoria and E. L. Dunlop claimed that the intramuscular route for administration of fluids to surgical patients has certain definite advantages. The time taken to insert an intramuscular needle is negligible, and this can be carried out by any intelligent assistant. In contrast to the intravenous route the danger of pulmonary oedema is remote, for, when the body has absorbed a sufficiency of fluid, the surplus accumulates as local oedema at the site of injection. The occasional difficulty of finding a suitable vein is obviated. Glucose can be given without any risk of necrosis, and phlebitis and generalized systemic infection associated with rigors are eliminated. The injection is given at the middle third of the lateral aspect of the thigh. A needle of 17 gauge and 4 inches long, with a tubing mount, is employed. The needle is fitted with a sliding adjustable shield, 1 inch by 1 inch, which can be clamped on any part of the needle with a fixing screw. For children or thin adults a shorter needle is more convenient. The needle is fixed by strapping the shield to the skin, and a piece of sterile gauze is placed between the skin and the shield. The part of the needle outside the thigh should be surrounded with sterile gauze. Both thighs may be injected simultaneously by employing a V-shaped glass connexion in the tubing leading from the flask holding the fluid. The rate of flow should be regulated by the requirements of the patient, a rate of about 40 drops a minute being suitable for most adults. The maximum of fluid given in 1 day by the authors, using both thighs, was 4,990 c cm. The needle must be inserted deeply, almost touching the bone.

Head Injuries

Aponeurotic transplantation—I. Lauwers recommends cranioplasty in the treatment of cranio-cerebral injuries. Various methods have been recommended. Of these the best is aponeurotic transplantation, completed by a cartilaginous graft. Jacksonian epilepsy is one of the late results of cranial injury. Scar tissue always forms. In simple wounds of the skull retraction of this is not serious. In cerebro-meningeal wounds, on the other hand, retraction may cause epilepsy.

Amniotic membrane—Yi-Cheng Chao *et al.* describe the use of amniotic membrane as a means of protecting the brain from superficial scars caused by injury, and so preventing adhesions. Thirteen materials were employed experimentally, including silver foil, mica, cellophane, fat, and fascia lata. Amniotic membrane, which appeared to be the most satisfactory, was prepared from fresh membranes from the delivery room. The membranes were washed in water to remove as much blood as possible. The inner membrane (the amnion) was freed from the outer (the chorion) by finger dissection, again washed in water, and placed in 70 per cent alcohol. It was then stretched and dried in sheets of convenient size. This was carried out by stretching on a smooth glass plate which had previously been rubbed over with a mineral oil. To remove the membrane from the plate, it was first moistened with 70 per cent alcohol. Sheets could be preserved dry, or in 70 per cent alcohol. Before use, the sheets were sterilized either by autoclaving for 20 minutes at 250° F. under a pressure of 120 lb., or by boiling in distilled water for 20 minutes. Membrane thus prepared, to which the name amnioplastin was given, was recommended as a routine covering to be interposed between the dura and the brain after craniotomy during which the brain had been exposed for a considerable time, or in cases of brain injury, as by removal of a tumour. In the treatment of brain wounds, after careful débridement, amnioplastin should be spread in an even layer over the wounded surface, in order to prevent adhesions. Amnioplastin remains as a foreign body for a short time, but is completely absorbed within 30 days.

Wounds of the Face

Primary suture—L. D. D. Davis emphasizes the importance of the immediate treatment of wounds of the face by operation and primary suture. Many patients arriving at a casualty clearing station are suffering from shock of varying degree and require rest and sleep. Unless haemorrhage continues or there is some urgent need for immediate operation, $\frac{1}{2}$ grain of morphine and $\frac{1}{100}$ grain of atropine should be given, then, after 2 hours of sleep and warmth, the patients are radiographed and sent to the operating theatre. The wound is thoroughly cleaned and loose fragments of bone and all accessible foreign bodies are removed. Efficient

drainage is established, and the mucous membrane and skin are sutured loosely and without tension by interrupted black synthetic horsehair or fine silkworm-gut stitches. Stitches are removed early, about the fourth day. If suppuration develops some stitches are removed. The author considers that early operative treatment and suture of face wounds before the inflammatory reaction occurs, prevent a considerable amount of suppuration, haemorrhage, deformity, and many tedious plastic operations. In fracture of the jaws only loose fragments of bone are removed, a fracture of the mandible will not unite if the teeth on each side of the line of fracture are not extracted. Wounds in the regions of the eyes and of the lips cause the greatest disfigurement.

Wounds of the Chest

Artificial pneumothorax —C. H. Kretzschmar describes wounds of the chest treated by artificial pneumothorax in the Spanish civil war. Though many wounds heal spontaneously without it, they often leave a damaged, inefficient lung. Nearly all penetrating thoracic wounds cause a pneumothorax and it is not necessary to make this total by operation unless it is valvular, infected, or accompanied by intrathoracic haemorrhage. Haemothorax, if present, should be emptied as completely as possible before the pneumothorax is induced, otherwise adhesions may form and there is the risk of infection. The pneumothorax stops or reduces the haemorrhage from the lung. A foreign body, if present, prevents damage from it by keeping the lung at rest. Kretzschmar considered that artificial pneumothorax has a definite place in the surgery of chest wounds during war-time.

Healing of Abdominal Wounds

Effect of local anaesthetics in oil —C. A. V. Burt and J. A. Criss discuss the effect of the use of prolonged anaesthetics in oil on the healing of abdominal wounds. In cats typical abdominal incisions were made into the peritoneal cavity, some without any local anaesthetic, others after the injection of plain almond oil, and others after the local infiltration of an anaesthetic in oil. Catgut and silk were used separately to close the deeper layers of all wounds, in all wounds catgut caused marked local inflammatory reaction, whether or not there was any local oil infiltration. There was slight reaction in wounds closed with silk. There was not any evidence that the presence of almond oil, plain or anaesthetic, in any of the wounds increased the incidence of discharge with either kind of suture material, or caused any delay in wound healing. That the oil in these wounds did not show any appreciable surrounding inflammatory reaction suggested the possible use of this form of infiltration anaesthesia in human incisions.

Wounds

Zinc peroxide —F. L. Meleney employed a suspension of zinc peroxide in the treatment of open wounds. After complete debridement the wound is flooded with a 40 per cent suspension of zinc peroxide in sterile distilled water, so that every part of the wound surface is in contact with the suspension. A double layer of fine-meshed gauze soaked in the suspension is then placed over the wound, gauze compresses and cotton-wool soaked in distilled water placed on top, and a final sealing is made with gauze impregnated with petroleum jelly. After 24 hours the dressing is changed, and the wound irrigated with saline without attempting to remove the zinc peroxide from the wound. Granulation commences on the third to the fifth day.

Aseptic pus —M. Belin and C. Belin employed aseptic pus for the treatment of wounds in animals, especially horses. They used pus from abscesses in horses, after bacteriological control this was emulsified in Ringer's solution with 0.5 per cent carbolic acid. This aseptic pus, in a dilution of 1 in 8, was injected subcutaneously into horses in doses of 5 to 10 c.cm.; the injections were repeated every 2 to 5 days. Local treatment was given. The local reaction was very slight, and there was no general reaction. Aseptic pus, in a dilution of 1 in 8, was injected subcutaneously in human subjects in doses of 2 c.cm. every second or third day, and proved to be very successful in the treatment of wounds, burns of the second degree, and certain infectious diseases.

Cellophane as dressing.—L. L. Howes reported satisfactory results from the use of

cellophane as a dressing for non-infected surgical wounds. Cellophane of a thickness of 0.0017 inch was employed. After preliminary sterilization by autoclaving, the material was cut to the requisite size in the operating theatre. It was then placed over the operation incision and fastened in place with strips of adhesive tape, the latter being applied along the edges of the cellophane in such a manner that it sealed them down. It was found that, if adequate haemostasis was obtained at the time of operation, small droplets of moisture and blood which collected under the cellophane covering during the first 24 hours, soon dried off. In cases in which excessive moisture collected after 24 hours, a small air vent was made in one corner of the cellophane, and covered by a piece of gauze. Only when haemostasis was inadequate as a result of some technical fault, such as incorrect approximation of the skin edges of the incision, did excessive accumulation of moisture occur. These cellophane dressings could be left on without cracking for 10 days. Advantages of cellophane over ordinary dressings were that the wound remained visible and so could be inspected without changing the dressing, they did not stick to the wound, they were more impervious to external bacterial contamination, and they were very economical.

New transparent bandage—M. Mituyasu described a transparent bandage which he has employed in place of plaster-of-Paris which in his view has the disadvantage of being heavy, and does not allow direct inspection of the area underneath. His transparent bandage was made up of acetylcellulose, 6 g., acetone, 90 c.c., methyl formate, 40 c.c., camphor, 2 g., and glycerin, 0.5 c.c. This mixture sets at a temperature of 60° C. and forms a firm, transparent film which is as hard as plaster, allows close inspection of the lesion, and is much lighter than plaster of Paris. Being painted on, it also allows easier adaptation to the skin. Unfortunately, it is not possible to use it for bigger joints, as the thickness required would impair translucency.

Cod-liver oil dressing—M. Lichtenstein studied the mode of action of cod-liver oil when used as a dressing. He found that staphylococci in a nutrient medium were destroyed by cod-liver oil in 2 weeks. *Bact. coli* in the same circumstances were unaffected. Adding vitamins A and D to the oil made no difference to these results. Liquid paraffin had no bactericidal effect on these organisms or on organisms not in a nutrient medium. Olive oil killed bacteria suspended in it in from 7 to 10 days, cod-liver oil in 17 to 22 hours, and boiled linseed oil in 1 to 1½ hours. Irradiation enhanced the bactericidal power of cod-liver oil which depends upon, among other factors, its content of peroxides.

Infected Wounds

Closed-plaster method.—J. D'Harcourt *et al.* report the results obtained from the closed-plaster method of treating war wounds in the Spanish war by Tructa and his co-workers. The advantages claimed from the method are: The period of healing, particularly that of the preliminary stage of disintegration, is greatly reduced, in wounds of the limbs a very high degree of conservative treatment is possible, with a consequent marked reduction in the number of amputations, strict immobilization of the wounds ensures a faster growth of epithelium, and obviates the non-union and the formation of callus in inconvenient sites which often follows extensive and infected open fractures; it eliminates the painful process of daily dressings, and prevents distribution and absorption of products of disintegration resulting from movements involved in the constant handling of the wound; secondary infections are avoided; proteolysis resulting from the use of antiseptics does not occur, and dehydration from evaporation at the surface of large wounds is greatly reduced. The method is as follows: If possible the wound should be cleaned out and excised within 6 hours of receipt. Infected wounds or those containing much necrotic tissue should be submitted to débridement and cauterization; the cavity of the excised wound should then be lightly packed with sterile gauze, which may be combined with petroleum jelly. A plaster bandage applied directly to the skin immobilizes the limb. The plaster should be carefully moulded over all bony prominences to ensure the greatest possible immobilization, and should enclose the two joints nearest to the wound. As a general rule the plaster should be left in position for from 3 to 6 weeks, without any window or opening made in it. A watch should be kept on the patient's general and local condition. Clinically the most important local indications

are a good circulation and range of movement in the fingers and toes, absence of oedema, normal temperature in the region of the wound, and freedom from all discomfort. The patient's temperature and blood counts should be watched, and radiograms should be taken to ensure that any fracture has been correctly reduced.

G. R. Girdlestone says that the success of the closed-plaster method of treating infected wounds depends for its success on the correct application to the individual case, on the judgment shown in the earlier processes, and on the perfection of the plaster work. The patient should be kept under supervision for 2 or 3 days, in order to make sure that the plaster is comfortable and that no untoward symptoms are developing.

J. Trueta and J. M. Barnes, describing the rationale of complete immobilization of the soft tissues in the treatment of infected wounds, said that experience had shown that such immobilization enabled the tissues of the body to resist invasion by many different varieties of bacteria, even when the latter continued to grow freely in the wound. Later, when the initial danger of invasion has been overcome, the cells and body fluids are capable of destroying these organisms and allowing the normal processes of repair to occur. The essential aim of this form of treatment is to provide the optimal conditions for the body itself to destroy the invaders, and no attempt is made to kill them by external agents.

Hypertonic sodium sulphate solution—J. C. Lyth (1940, a) claims that hypertonic sodium sulphate solution provides a wound dressing far superior to any hitherto employed. No other hypertonic agent approaches sodium sulphate in efficiency. A saturated solution of sodium sulphate (Glauber's salt) is made by placing about 2 lb. of the salt in a winchester bottle, filling with cold reasonably sterile water, and shaking. As the solution is used, more water is added, so long as undissolved crystals remain. The surface of infected wounds is kept in contact with plain lint, or cotton wool in the case of deep irregular cavities, and covered with elastoplast, or oiled silk or grease-proof paper. Fresh clean non-penetrating wounds are not washed with water or antiseptics, but bathed gently with the solution. A dressing soaked in the solution is then applied and left in position for 24 hours or longer, if there is no pain, fever, or discharge. Before removing, the dressing is again soaked in the solution. If no inflammation occurs, the dressing is repeated. If the wound becomes septic, or is already septic, obvious foreign bodies are removed without disturbing exposed tissues. The dressing should be soaked more frequently, hourly if necessary, by turning back a corner of the elastoplast or oiled silk covering. Important adjuncts to treatment are elevation of a limb by sling or foot-rest, and immobilization by splints or plaster.

This author reports (1940, b) the results obtained from the extensive use of a hypertonic saline solution alone applied to the surface in 1,096 cases of septic infection. No bactericidal antiseptic was employed in any case. The author found that septic conditions cleared up with astonishing rapidity under this treatment.

Embryonic extract—W. G. Waugh summarizes the work on this subject carried out in tissue cultures by Carrel and his colleagues, and reports the results obtained in 18 patients, 4 of which are described in detail, by the application of a sterile, stable embryonic extract to wounds. This protein derivative of embryonic tissue, adsorbed on kaolin, is called epicutan, was prepared under the supervision of A. Fisher, Director of the Carlsberg Biological Institute of Copenhagen, and was about to be marketed in Great Britain before the outbreak of war. The wound is powdered and covered with sterile gauze and dressed every 5 days. In addition the author immobilized the area of the wound because this alone appears to inhibit a flare-up of infection, though it does not alone influence the healing tissue. Graphs constructed from measurements, made at Copenhagen, of the healing process by Du Noy's formula showed that a noticeable delay in healing followed an inter-current disease. This mathematical method of measuring the rate of healing was used in 2 of the author's cases, and confirmed the conclusion that epicutan reduced the time of healing by 30 per cent.

Local application of sulphanilamide—V. Chorine reports the use of *para*-aminosulphanilamide (1162 F) as a local application in wounds, recent and infected, and in opened abscesses and boils, in 50 cases in all, with remarkable success. Before the local application of a paste made of the powder with a little water, or simply

sprinkling the drug in a dry powder, over the wound, it is important to clean the recent wound thoroughly, tetanus antitoxin being given if such protection has not been previously provided as in the army, necrotic tissue and blood clot are also removed. After 24 hours the cleansing process is repeated and removal of necrotic material again carried out. Unless this preliminary is insisted on, infection follows in a few days. As a solution of hydrogen peroxide acts on the drug, its use is inadvisable. In 31 recent wounds thus treated, the powder being applied to the wound and all its branchings after the 24 hours' interval, infection did not follow. In wounds infected when they first come under observation, the same technique is employed, except that the cleansing must be repeated every day. Cases of old suppuration respond well to this treatment. A. Szary had treated an extensive gangrenous lesion in man by this method with success. Nitti reported that the local application of 1 g of 1162 I per kilo of body weight in wounds contaminated with virulent streptococci had a remarkably beneficial effect in rabbits.

Maggot therapy. The therapeutic effect of maggots in producing healing of infected wounds has been ascribed, not merely to the scavenger action of the maggots, but to allantoin, a metabolic product present in the maggot secretions. Urea has also been shown to have a similar effect. W. Robinson, in a further analysis of the secretions of surgical maggots, found that ammonium bicarbonate was present in comparatively large quantities. With the aid of a number of physicians and surgeons solutions of both ammonium bicarbonate and ammonium carbonate were employed clinically, and found to have marked healing properties similar to those of the other two maggot products, allantoin and urea. Gauze packs saturated with 1 to 2 per cent sterile solutions were employed, or irrigations of these solutions were made. This treatment was employed with excellent results in purulent conditions such as varicose and diabetic ulcers, chronic osteomyelitis, slow-healing abdominal wounds, abscesses, otitis media, and infected lacerations. Improvement in the condition of the wound began after a few days' application, offensive odour rapidly decreased, the wounds became cleaner, small areas of fresh granulations could be seen in the wounds, and later a general development of granulation tissue generally occurred.

Hypoproteinaemia

Prevention and control in surgical patients. I. S. Ravdin *et al.* investigated the prevention and control of hypoproteinaemia in surgical patients. Lack of protein may lead to a delayed healing of wounds and to oedema. A high-carbohydrate high-protein diet given by mouth is the best means of preventing hypoproteinaemia before operation. A suitable diet contains approximately 70 to 80 per cent of carbohydrate, 20 to 30 per cent of protein, and 5 to 10 per cent of fat. If the food cannot be retained or if it cannot be absorbed by the stomach, it must be given by another route. Amino-acids or lyophile serum may be given intravenously to raise the serum protein. Normal serum is also efficacious. The alimentary route being better, most patients will tolerate food given by the orojunal method. As a rule from 65 to 90 g. of protein, and from 200 to 300 g. of dextrose were fed daily. In addition, sufficient sodium chloride and water were added to maintain a normal level of the plasma chlorides and a normal fluid volume. If this is impossible peptone hydrolysate may be given by rectum, but it is not so efficacious.

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INTESTINAL OBSTRUCTION

See also B.E.M.P., Vol. VII, p. 221, Cumulative Supplement, Key Nos. 761-775
 Surveys and Abstracts 1939, p. 387 and p. 12 of this volume

Acute Intestinal Obstruction

Extra-Abdominal Hernias

J. M. Miller discussed internal hernias as a cause of intestinal obstruction. These are considerably rarer as a cause of intestinal obstruction than external hernias. Of 39 intra-abdominal hernias at the Mayo Clinic 28 showed obstruction, and in 19 of these it was acute. It is a not uncommon sequel of gastro-enterostomy. Any openings in the mesocolon or peritoneum should therefore always be closed with the greatest care. Excessively drastic operations for retroversion are another potential cause of internal herniation. Paraduodenal hernias only occur in two well-recognized fossae—the left paraduodenal fossa of Landzert and the mesenterico-parietal fossa of Waldeyer. Congenital abnormalities very occasionally give rise to internal hernias. The typical picture of an obstructed internal hernia is acute obstruction, together with a localized abdominal swelling which is resonant to deep percussion and over which borborygmi can be heard.

Intussusception

Radiological diagnosis and treatment. After a review of the literature, and with a personal radiological experience of 15 cases, of infants, children and adults, since 1933, L. R. Williams advocates a wider use of radiological methods, not only as a certain means of diagnosis, but also as a highly useful and controlled form of treatment. The forms of intussusception are classified anatomically as follows: (i) enteric or ileo-ileal (10-15 per cent) usually in infants and children, often due to a polyp or an inflamed Meckel's diverticulum, and confined to the small intestine; (ii) colic or colo-colic (5-10 per cent), usually in adults and often associated with the presence of a tumour; (iii) entero-colic (75-80 per cent) the most important group both in early life and adults, is divided into (a) ileo-caeco-colic, the ileo-caecal valve forming the apex, and (b) ileo-ileo-colic, beginning in the terminal ileum and progressing through the ileo-caecal valve with a changing apex. Aetiological peak of incidence coincides with the age of weaning, i.e. 6 to 8 months. In infants and children the condition is acute or less often subacute, whereas in adults it is usually chronic and often associated with a tumour. In acute intussusception in early life an accurate diagnosis is obtained by a barium meal in all cases except those of the ileo-ileal form. If the diagnosis is uncertain, a barium enema should be given. Even when the clinical diagnosis is certain, a barium enema is a valuable form of treatment in all but advanced cases and may render operation unnecessary, or, if necessary, make it easier. In subacute and chronic cases in adults the most precise pre-operative diagnosis of the presence and cause of the invagination can be obtained from combined contrast meal and enema examination.

By Remnants of Vitelline Vascular System

J. S. Buchanan and H. Wapshaw recorded 2 cases of obstruction of the small bowel caused by remnants of the vitelline vascular system. In 1 case, that of a man of 20, the patient was seized with acute abdominal pain of a colicky nature, following a normal stool. Vomiting occurred early and soon became faecal in character. There was absolute constipation. There was a history of 2 previous attacks of a

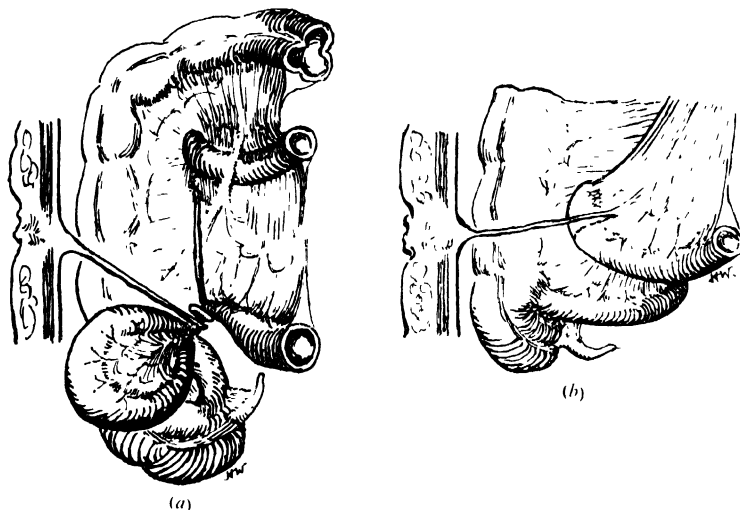


FIG. 10—(a) Persistent right vitelline vein disappearing below the third part of the duodenum, after having ensnared a loop of the small bowel; (b) Remnant of the vitelline artery, attached at umbilicus and upper surface of mesentery. (From *British Journal of Surgery*, 1940.)

similar, though less severe, nature. The patient showed the other usual signs of intestinal obstruction. On opening the abdomen the obstructive element proved to be a stout plum-coloured cord, which almost certainly was a remnant of the right vitelline vein. In the second case, that of a schoolboy of 12, there was a history of intermittent attacks of colicky pains, at intervals of 3 weeks, during the previous 3 months. On operation a string-like band was found which appeared to be a remnant of the vitelline artery.

Obstruction of the Small Intestine

Influence of Nervous System

J. Fine *et al.*, from an investigation into the part played by the nervous system in acute intestinal obstruction, concluded that the survival time of cats with gaseous distension of the small intestine was inversely proportional to the level of the pressure in the intestinal lumen. Preliminary exclusion of the intrinsic nervous supply of the gastro-intestinal tract did not influence the survival time of such animals. Fluid accumulation in the lumen of the intestine, bowel wall, and peritoneal cavity in these animals was not sufficient to account for their rapid death. Extrinsic denervation of the gastro-intestinal tract did not significantly alter the fluid volume in the intestine or peritoneal cavity.

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Malignant Disease of the Duodenum

Duodenal Carcinoma

D. N. MacCharles records an unusual case in which primary carcinoma occurred in the first part of the duodenum and not in the second. A man, aged 53, was operated upon, and a mass, the size of a small grape-fruit, was found near the pylorus; owing to the patient's condition it was decided to perform posterior gastro-enterostomy only. Great improvement followed, and 5 months after the onset of symptoms a second laparotomy showed that the mass left at the first operation had almost entirely disappeared, but a rather large ulcer in the first part of the duodenum near the junction with the second was found. The distal end of the stomach and the proximal portion of the duodenum were excised, and it was then concluded that the original mass was inflammatory. The pathological examination, however, showed that the ulcer was carcinomatous.

Leiomyosarcoma

S. W. Harrington and J. A. Ganshorn record a leiomyosarcoma of the third part of the duodenum in a woman, aged 38, who was anaemic, tired, and had occult blood in the faeces. A stasis radiogram showed a flat polypoid tumour at the junction of the second and third parts of the duodenum. At laparotomy an elliptical tumour measuring 4 by 2.5 by 2.5 cm. with ulceration of the mucosa was successfully removed. Benign tumours of smooth muscular tissue in the stomach and small intestine have been divided into: (i) small multiple nodular or polypoid tumours arising from proliferation in the muscularis mucosae, the mucosa being free from invasion; (ii) broad thick tumours arising from the muscular coats of the intestine with adhesion to the mucosa; and (iii) larger, polypoid subserous myomas projecting into the peritoneal cavity. There has been some controversy about the nature of malignant change in leiomyomas, and many, probably the majority, are malignant from the start. Sarcoma arising in the duodenum is much rarer than primary carcinoma.

Harrington, S. W., and Ganshorn, J. A. (1940) *Proc. Mayo Clin.*, **15**, 74.

MacCharles, D. N. (1940) *Canad. med. Ass. J.*, **42**, 573.

Post-Operative Intestinal Atony

Treatment

Prostigmin. P. A. Marden and I. G. Williamson found that prostigmin, given prophylactically both before and after operation, effectively reduces the incidence of post-operative intestinal atony and urinary bladder retention. They employed the drug in 253 operative cases, of which 250 were studied for intestinal distension and 247 for urinary retention. In both groups some patients received the drug before and after operation, some before operation only, and some after operation only. In the first 2 sub-groups the drug was given in 3 injections over the period of 18 hours before the operation; in the first and third groups it was begun within 4 hours of the patient's return from operation, and continued at 4 or 6 hour intervals for a total of 4 to 6 doses, or more, if distension or retention appeared imminent. A dosage of 1 c.cm. of a 1 in 4,000 solution was generally found sufficient but, if this appeared to be insufficient, 1 c.cm. of a 1 in 2,000 solution was employed. In the first and second sub-groups combined, in which the drug was given before operation, the incidence of intestinal distension was reduced to 5.7 per cent; in the third sub-group the incidence was 14.4 per cent. In the urinary retention series those patients receiving the drug before operation required catheterization in only 3.9 per cent of cases, while 6.9 per cent of those receiving it after operation had to be catheterized. No ill-effects from the drug were noted.

Marden, P. A., and Williamson, I. G. (1939) *Surg. Gynec. Obstet.*, **69**, 61.

INTESTINES, TUBERCULOSIS

See also B. E. M. P., Vol. VII, p. 253, and Surveys and Abstracts 1939, p. 389.

Treatment

Calcium Gluconate

V. V. Pisani employed calcium gluconate by intramuscular injection in 43 cases.

of intestinal tuberculosis. The dosage was 10 c cm. of a 10 per cent solution, given 3 times a week, over periods of from 6 to 25 months, with an average of 13 months. Of the 43 patients, 20 were definitely improved, i.e. major symptoms such as nausea, vomiting, diarrhoea, and abdominal cramps were definitely lessened in severity, if not completely relieved, 13 were fairly improved, i.e. there was lessening of symptoms with slight improvement of appetite, weight, strength, and general appearance, and 10 were not improved. The author concluded that calcium therapy is worthy of use in intestinal tuberculosis.

Pisani, V. V. (1939) *Amer. Rev. Tuberc.*, **40**, 571.

INTRAVENOUS TRANSFUSIONS

Emergency Method of Preparing Pyrogen-Free Water

J. C. Lees and G. A. Levy described a method whereby, in a civil or military emergency, tap-water or unsatisfactory distilled water could be readily freed from pyrogens and rendered suitable for the preparation of intravenous infusions. A typical pyrogenic reaction consists of a rigor and feeling of chill at any time between 15 minutes and 8 hours after the injection. The reaction is followed by profuse sweating, and a fall in temperature, and there may also be nausea, vomiting, headache, and albuminuria. The method of removing pyrogens consists of shaking the water for 15 minutes with powdered activated charcoal, 1 part per 1,000, this removes pyrogens from heavily contaminated water. The charcoal can be readily removed by allowing the liquid to stand for a few minutes, and then decanting through a fluted filter-paper. The receiving vessel, which must be spotlessly clean, should be washed out with a little of the filtrate before collecting the remainder.

Lees, J. C., and Levy, G. A. (1940) *Brit. med. J.*, **1**, 430.

JAUNDICE

See also B. E. M. P., Vol. VII, p. 261; Cumulative Supplement, Key Nos. 779-788; Surveys and Abstracts 1939, p. 389; and p. 28 of this volume.

Diagnosis

Estimation of Diameter of Red Blood-Cells

L. Schalm claimed that increase in the size of the red blood-cells provides a valuable means of differentiating types of jaundice. An increase in the mean diameter of 1.0μ or more indicates the great probability of considerable destruction, or an important functional alteration of the liver tissue, which may itself be the cause of the jaundice without any obstruction of the main biliary passage. In exceptional cases a similar increase in size of the red cells may occur in certain cases of carcinoma of the head of the pancreas without severe involvement of the liver. An increase in diameter of 1.0μ or more in cases of jaundice almost certainly rules out the diagnosis of obstruction due to calculi in the biliary tract without severe liver damage.

Schalm, L. (1940) *Pr. méd.*, **48**, 312.

The Hepato-Renal Syndrome

T. G. Orr and F. C. Helwig report 5 cases suggesting that in the presence of hepatic damage a toxin acts upon the kidneys. The urinary output is decreased, albumin, casts, pus, and often red blood-cells appear in the urine, and the blood non-protein nitrogen and creatinine are increased. A high temperature was present in all the cases and delirium in 4. Two of the cases proved fatal, and at necropsy cloudy swelling of the renal parenchyma and congestion of the glomeruli were found. The nature of the toxin is unknown, but these changes are almost certainly not due to infection. Severe liver trauma should be treated by operation to control the bleeding, and by administration of dextrose to preserve the liver glycogen and promote diuresis.

Orr, T. G., and Helwig, F. C. (1939) *Ann. Surg.*, **110**, 682.

In an article, entitled 'Supplementary Contributions to the Clinical Information about "Hepatorenale Erkrankungen"', S. Tsuji of Matsuo Clinic of the Imperial University, Kyoto, describes cases in which both the liver and the kidneys are damaged at the same time, for example, spirochaetosis icterohaemorrhagica, which is an acute form. He, however, classifies the form as follows—Acute, serious and slight and chronic—following Matsuo, who described the combination of hepatic cirrhosis and nephrosis. mention is also made of hepatonephritis in the course of tertiary syphilis. A special account with 5 illustrative cases is given of mild acute cases, as distinguished from the severe form of spirochaetosis icterohaemorrhagica, the patients included various forms of infection—erysipelas, scarlet fever, influenza, tonsillitis, and presented symptoms such as jaundice and hepatic enlargement and nephritis and pyelonephritis. It is suggested that F. ppingers so-called 'serose Entzündung' in most cases shows hepatonephritis.

F. ppingers, H. (1937) *Die Leberkrankheiten*, Vienna.

Tsuji, S. (1939) *Jap. J. Gastroent.*, **11**, 147.

Obstructive Hepatic Jaundice

Hypoprothrombinaemia

Synthetic vitamin-K therapy.—H. A. Frank *et al.* employed synthetic vitamin K₁ (2-methyl-3-phytyl-1,4-naphthoquinone) in the treatment of the clinical hypoprothrombinaemia in 2 cases of obstructive jaundice, both orally and intravenously. By the intravenous route the synthetic vitamin was given as a freshly-prepared colloidal suspension in 10 per cent glucose. This solution was prepared by dissolving 10 mg. of the oil in 2 or 3 c.cm. of absolute ethyl alcohol, which was then added slowly to a sterile solution of 1,000 c.cm. of 10 per cent glucose in distilled water. To 3 normal human subjects, 1,000 c.cm. of the freshly prepared solution (representing 10 mg. of the vitamin) were given intravenously; no reaction was noted and there was no significant change in the normal prothrombin level, or in the clotting or bleeding times. In 1 case of obstructive jaundice, due to a malignant growth involving the gall-bladder, and with an elevated prothrombin clotting time, 10 mg. of synthetic vitamin K₁ by mouth on 2 occasions produced a drop which was maximal at the end of 24 hours. Given intravenously the vitamin produced a fall to normal level within 4 hours. Twenty-four hours after injection, a further 10 mg. was given together with bile salts by mouth, to prepare the patient for operation on the following day. At no time during the operation, or in the post-operative period, was abnormal bleeding noted, and the prothrombin time remained normal until the patient died 3 days after operation. In the second case, a single intravenous dose of 10 mg. resulted in a fall in clotting time which lasted for 6 days.

Control of Post-Operative Bleeding

Vitamin K and cholic acid.—J. D. Stewart *et al.* report 2 cases of jaundice in which the prothrombin level was very low after operation. The administration of vitamin K-cholic acid mixture raised it to normal, and stopped excessive bleeding. Other illustrative cases were reported. Post-operative bleeding in obstructive jaundice has been shown to be caused by a reduction in plasma prothrombin. For the manufacture of prothrombin, vitamin K must be absorbed in the presence of bile. In jaundice several factors may prevent this manufacture, such as lack of bile salts and intake of insufficient food containing the vitamin. During obstructive jaundice the prothrombin stores are depleted. Anaesthesia also depresses the blood-level and, since the patient has no stores to call upon, the level is very low after operation. The response to therapy is better when the obstruction is due to stone than when it is due to carcinoma, and possibly greater liver damage occurs in carcinomatous obstruction. Large doses of vitamin K are necessary in this condition. In treating prothrombin deficiency in obstructive jaundice it is also necessary to give an adequate intake of carbohydrate and other vitamins. Proper fluids and blood transfusion are also important.

J. D. Stewart and G. M. Rourke, in an investigation into the causes of prothrombin deficiency in obstructive jaundice, found that the longer the duration of the jaundice and the greater the liver damage, the lower is the prothrombin level. Vitamin K-cholic acid mixtures raise the level to normal and it does not exceed normal even if

the treatment is continued. In the same way administration of the mixture to normal individuals does not raise the level above normal. A reduction in prothrombin of 20 to 30 per cent was usually seen after operation. This was probably due to such factors as loss of blood and cessation of the intake of vitamin K. In treating prothrombin deficiency it is also important to give the patients dextrose and fluids and to relieve the obstruction to the bile-ducts as soon as possible.

Frank, H. A., Hurwitz, A., and Seligman, A. M. (1939) *New Engl. J. Med.*, **221**, 975.

Stewart, J. D., and Rourke, G. M. (1939) *J. Amer. med. Ass.*, **113**, 2223.
and Allen, A. W. (1939) *Ann. Surg.*, **110**, 693.

Toxic and Infective Hepatic Jaundice

Spirochaetosis Icterohaemorrhagica

S. Tokuyama observed 12 cases of spirochaetosis icterohaemorrhagica (Weil's disease) in Hawaii, the diagnosis of which was confirmed clinically in 2 cases and bacteriologically in 9. The disease proved to be identical with that occurring in Japan. Of the 12 cases, 9 were injected with Inada and Ido's serum, of these, 7 recovered and 2 died. Of the 3 patients who did not receive the serum, 2 died. The serum was given, according to Inada and Ido's technique, in a dosage of 40 c.c.m.

Nervous complications.—V. Mortensen reports a case of spirochaetosis icterohaemorrhagica (Weil's disease) in a man, aged 59 years, complicated by meningitis and complete paralysis of the lower limbs. The patient ultimately recovered and could walk almost normally. Serological reactions showed that the patient was infected with *Leptospira icterohaemorrhagiae*. Meningitis has been stated to be not uncommon, and in some forms it is more predominant than the jaundice. In 1 case the spirochaete has been cultured from the cerebrospinal fluid. Paralysis of the lower extremities, indicating an extension to the nervous parenchyma, is very rare. Mortensen found 4 reported cases only. A more severe infection of the cerebral parenchyma is very rare, but lesions in the peripheral nerves have been noted.

Rapid presumptive serological test.—H. C. Brown described a rapid presumptive serological test for Weil's disease. Small quantities of varying dilutions of the patients' serum are rocked to and fro on a slide in the presence of a heavy suspension of *L. icterohaemorrhagiae*. This suspension is made by centrifuging at high speed about 500 c.c.m. of a massed culture after the addition of formalin to a concentration of 0.2 per cent and saponin to a concentration of 1 in 1,000, collecting the deposit and suspending in saline until the opacity approximates to that of a No. 1 Wellcome opacity tube used for the standardization of vaccines. Equal quantities of the serum and antigen are rocked for 10 minutes and the result is read with a hand lens against a dark background. The test can be read macroscopically after incubation for 3 hours in a water-bath at 56°C. These tests have been found reliable on many occasions in a titre as small as 1 in 10. If the test is positive, curative serum may be given at once.

Catarhal Jaundice

J. Schwartzman and A. Maffia reported 35 sporadic cases of catarrhal jaundice. The condition is usually thought benign, but fatalities have been reported. The jaundice may be due to obstruction to the bile by swelling of the mucosa in the common duct. The cause of the condition is unknown. When epidemic, it may be spread by droplet infection and it may be due to a virus or spirochaete. In this series the greatest number of cases occurred in summer and winter. There were 19 females and 16 males. The commonest age for infection was 3 to 11 years. The onset was usually accompanied by a gastro-intestinal disturbance, but in 10 cases an upper respiratory infection occurred. With the onset of jaundice these symptoms disappeared and recovery was uneventful. The icteric index was raised, and it was found the most reliable method of testing for jaundice. It gave a positive result earlier than the van den Bergh reaction or examination of the urine. Other laboratory examination showed the blood sugar to be slightly lower than normal, the sedimentation rate to be normal, the cholesterol level raised, and the cholesterol esters diminished. Blood counts varied, but a leucopenia with a relative lymphocytosis

occurred in most. The fragility of the red cells was within normal limits. Of the patients 26 received a high-carbohydrate diet, 5 a high-fat diet, and 4 a regular ward diet. The effect of these treatments was judged by means of the icteric index therapeutic quotient, i.e.

$$\frac{\text{Highest Icteric Index}}{\text{Total Duration of the Disease}}$$

The results of the different diets were practically identical. None of them had any adverse effect on the gastro-intestinal symptoms. However, the best results were obtained with the regular diet, the next best with the high-carbohydrate diet, and the least good with the high-fat diet.

Vitamin-A absorption. B. B. Breese and A. B. McCoord investigated 21 patients with catarrhal jaundice from the point of view of vitamin-A absorption. In patients whose absorption is normal the maximal amount of vitamin A in the blood was found, 4 hours after ingestion of a high-potency fish-liver oil, to average 170 blue units of vitamin A per 100 c.c. of blood. In most of the cases of catarrhal jaundice this normal absorption did not occur. It was found, however, that, as the disease improved, the rise of vitamin A in the blood after ingestion was equal to, or higher than, that of normal persons. The author stated that bile salts probably aided in the absorption of vitamin A, when given by mouth to patients with catarrhal jaundice.

Diagnosis—a new test. J. Paraf *et al.* describe a new test for the determination of hepatic insufficiency, which they have made in an obscure case of jaundice in which the icterus—otherwise with the common symptoms of catarrhal jaundice—was not accompanied by an oliguria and also differed with regard to the results of the authors' new test.

The authors discuss the aetiology of catarrhal jaundice and conclude that in their case it is probably an icterogenic hepatitis. If this icterus had been caused by an insufficiency of the liver (allergic state), an injection of histamine would probably have exacerbated the symptoms in accordance with an experiment by Tzanck *et al.* After the injection there was a galactosuria of 15 per cent compared with a normal concentration of galactose of 5 to 6 per cent.

After this observation, histamine provocation was induced in 26 cases. In 12 normal patients (8 ill but not suffering from liver diseases) the percentage of galactose remained the same after injection of histamine as before. In 6 cases of cirrhosis without jaundice there was a strong reaction to histamine injection. The 8 patients suffering from icterus due to carcinomatous obstruction, cholelithiasis, and of the catarrhal type (4 patients) are discussed in detail. The patients with carcinoma of the pancreas and of the bile-ducts did not show any increase in the galactose excretion after histamine injection. The same was the case with the 2 patients with obstructive jaundice.

One of the patients with catarrhal jaundice showed a doubling of the galactose content of the urine in 24 hours after histamine injection. The second patient had no galactosuria but excreted about 2 per cent after provocation with histamine. The 2 other cases did not show any increase of galactosuria after histamine.

The authors point out that in cases in which histamine provocation produces an increase of galactosuria the cause of the jaundice is allergic.

Breese, B. B., and McCoord, A. B. (1940) *J. Pediat.*, **16**, 139.

Brown, H. C. (1939) *Brit. med. J.*, **2**, 1183.

Mortensen, V. (1940) *Lancet*, **1**, 117.

Paraf, J., Klotz, E., and Lewi, S. (1939) *Bull. Soc. méd. Hop. Paris*, **55**, 1087.

Schwartzman, J., and Maffia, A. (1940) *Arch. Pediat.*, **57**, 181.

Tokuyama, S. (1940) *J. Amer. med. Ass.*, **114**, 2195.

Tzanck, A., Sidi, E., and Dobkevitch (1938) *Soc. franç. Derm. Syph.*, **45**, 401.

Treatment

Sulphamylamide in Presence of Jaundice

W. H. Cleveland stated that, although jaundice and the evidence of liver damage

are usually taken to be contra-indications to sulphanilamide therapy, some cases have been reported in which it has been safely used in their presence. He reported a case of severe post-operative cholangitis occurring in a woman whose liver had previously been damaged by obstructive jaundice and biliary cirrhosis caused by a stricture of the common bile-duct. The patient had been the subject of a cholecystoduodenostomy and on the ninth post-operative day developed a high temperature, abdominal pain and a great enlargement of the liver. She was given 45 grains of neoprontosil by mouth and 150 grains of sulphanilamide subcutaneously in the first 48 hours. Her condition improved and subcutaneous treatment was continued until the fortieth post-operative day. On the sixty-seventh post-operative day the patient left hospital recovered. Cleveland concluded that sulphanilamide could be used in these circumstances if there were some infection present for which it was indicated.

Cleveland, W. H. (1939) *Proc. Mayo Clin.*, **14**, 680

JOINTS, DISEASES AND DISORDERS

See also B I. M. P., Vol. VII, p. 278, and Surveys and Abstracts 1939, p. 390

Loose Bodies

Osteochondritis Dissecans

R. Chierici discussed the aetiology of osteochondritis dissecans, first described by König in 1887 and characterized by the formation of a loose body or loose bodies in a large joint, generally the knee, though the hip and elbow joint are sometimes the site. The author dismisses the hypothesis of non-vascular necrosis and thinks that all cases must have been preceded by trauma, however slight. He emphasizes this opinion by observations on his own cases and by a number of radiographs.

Osteochondritis Dissecans of Hip

D. King and V. Richards stated that osteochondritis dissecans is as distinct an entity in the hip, as in the knee or elbow. Diagnosis can be made only by X-ray examination. For proper visualization and removal of the osteochondritic focus, dislocation of the femoral head from the acetabulum is necessary. Despite the controversial risk of favouring later arthritic or necrotic changes in the head of the femur, surgery gives definite symptomatic relief, and may prevent the development of *malum coxae senilis*.

Foreign Body Activity

J. A. Key reports 5 cases of chronic arthritis due to bullets (2 cases), a thorn, a needle, and a piece of glass, and states that if a foreign body remains in a joint or even is embedded in the synovial membrane near the joint surface, a progressive degenerative arthritis may be expected. R. B. Osgood and M. N. Smith-Petersen both drew a distinction between the effects of irritative and of inert foreign bodies; the large vitalum moulds used by Smith-Petersen did not cause any irritation.

Prognosis after Removal

R. Leriche *et al.* report the late results of removal of loose bodies in 12 cases of osteochondritis dissecans, in 8 cases of synovial osteochondromatosis, in 9 cases of traumatic foreign bodies, and in 2 cases of loose bodies formed in arthritic joints. In osteochondritis dissecans the late results were excellent, and in many of the cases some healing of the defect took place, only 3 showed any chronic arthritis. There were excellent results in 2 of 3 cases of osteochondromatosis which were followed up. Five of the cases of foreign body due to intra-articular fractures showed good results on re-examination in from 3 to 10 years after operation.

Chierici, R. (1939) *Quad. radiol.*, **17**, 43.

Key, J. A. (1939) *J. Amer. med. Ass.*, **113**, 1065.

King, D., and Richards, V. (1940) *J. Bone Jt. Surg.*, **22**, 327.

Leriche, R., Jung, A., and Berthel, C. (1939) *J. Chir., Paris*, **54**, 1.

- Osgood, R. B. (1939) *J. Amer. med. Ass.*, **113**, 1066
 Smith-Petersen, M. N. (1939) *J. Amer. med. Ass.*, **113**, 1066.

Knee-Joint

Chondritis

W. Darrach points out that failure to cure internal derangement of the knee by removal of a meniscus through a small incision shows that it is advisable to make an incision large enough to allow thorough exploration of the knee-joint. The most frequent associated condition is an alteration of the articular cartilage covering the femur, patella, and tibia. The first manifestation is a change in colour and firmness, instead of bluish-white the cartilage appears yellow; it feels softer when pressed with a blunt instrument and, when the latter is moved along the surface, the cartilage rolls up in front of it. Detached small fragments are found lying about the joint cavity, or larger pieces are either free or partially attached. The author considers the term *chondritis* more suitable than *osteo-chondritis*. The average age of the author's patients was 33 years, and the condition is regarded as a response to trauma, rather than the result of a general condition, or of some disturbance of subjacent blood supply.

Darrach, W. (1939) *Ann. Surg.*, **110**, 948.

Post-Traumatic Atrophy

R. K. Ghormley describes post-traumatic painful atrophy of joints which he considers to be related to Sudeck's atrophy and to disuse atrophy. The joints most commonly affected are the knee and ankle, though the shoulder and the wrist may be involved. Only one joint is usually affected in the same individual. The condition may simulate tuberculous arthritis, but there is little or no free fluid in the joint. Radiography reveals a punctate or diffuse osteoporosis without any changes in the outline of the joint. Massage and graduated exercises usually hasten improvement, while calcium and vitamin-D therapy may prove of value.

Ghormley, R. K. (1939) *Arch. phys. Ther.*, **20**, 725.

Tumours of the Synovial Membrane

Malignant Synovioma

In a malignant tumour of the synovial membrane with metastases in the lungs and pleurae, D. H. Kling found hypertrophy of the synovial cells in the highest degree forming gland-like structures containing synovial fluid in their lumina; the connective-tissue cells of the synovial membrane also showed sarcomatous change. Kling's hypothesis of the dual structure and function—capsular and secretory (mucin)—of the synovial membrane elucidates the complicated structure of the malignant synovioma. The opinion that the synovial membrane, being mesenchymal in origin, cannot secrete is dismissed as antiquated.

Kling, D. H. (1939) *The Synovial Membrane and the Synovial Fluid*, London, p. 80.

JOINTS, INJURIES AND INTERNAL DERANGEMENTS

See also B. F. M. P., Vol. VII, p. 321 and Surveys and Abstracts 1939, p. 392.

Penetrating Wounds

Treatment

Primary closure.—A. Basset stated that, if penetrating wounds of joints can be adequately dealt with in a properly equipped hospital within 8 to 10 hours of the injury, the function of the joint can be best preserved by primary closure of the synovial wound. Before operation, an X-ray should be taken to ascertain the extent of bone damage. Operation should be performed under spinal or general, never local, anaesthesia. The skin wound should be carefully excised back to the healthy tissue. If the skin wound does not permit careful exploration of the articular cavity,

the primary wound should be closed and a typical arthrotomy incision made. The joint should be carefully washed out, and all blood clots and bone fragments removed. The joint should then be closed by primary suture.

Basset, A. (1939) *Pr. méd.*, **47**, 1493

Degenerative and Proliferative Changes

Cysts of Semilunar Cartilages

Aetiology. I. S. McReynolds stated that mucoid degeneration and trauma are probably factors in the aetiology of cysts of the semilunar cartilages. The condition is considered by most authors to be congenital. Most cases occur in males, and the outer third of the external cartilage is chiefly involved. The symptoms include moderate pain and swelling about the joint and tenderness on deep pressure. The chief diagnostic points are location of the mass at the level of the joint and its movement with the tibia when the joint is moved. Treatment consists of complete extirpation of the cyst with removal of the entire affected cartilage. If the latter is not removed, recurrence takes place.

McReynolds, I. S. (1939) *Sth. med. J.*, **32**, 57

Traumatic Derangement of Joints

The Knee-Joint

Prognosis after removal of the menisci. I. Hfskind described follow-up observations on a series of 32 patients who had had the menisci removed from the knee, some as long as 5 years previously. X-ray examination with the patient in the upright position showed that there was lessening of the joint-spacing both immediately after the operation and at later periods. When arthritis had occurred there was no lessening of the joint-space. The author concluded that the meniscus does play a part in the supporting mechanism of the condyles of the femur, that, if regeneration of the meniscus does occur, its structure is inferior to that of the one removed, and that post-operative effusion increases the incidence of arthritis.

Hfskind, L. (1939) *Acta chir. scand.*, **82**, 499

KALA-AZAR

See also B. L. M. P., Vol. VII, p. 330, and Cumulative Supplement, Key No. 826

Diagnosis and Differential Diagnosis

Sternal Puncture

D. G. Reddy and R. Subramaniam consider that sternal puncture in kala-azar, as a method of demonstrating the presence of Leishman-Donovan bodies, is markedly inferior to splenic puncture, and that a negative sternal puncture should always be supplemented in doubtful cases by a splenic puncture. They quote 11 cases of kala-azar, in 2 of which, after the sternal method had been used, a 2-hours search failed to reveal Leishman-Donovan bodies which were subsequently seen with great ease after a splenic puncture.

Reddy, D. G., and Subramaniam, R. (1939) *Indian med. Gaz.*, **74**, 664

Treatment

4'-diamidino stilbene

A. R. D. Adams and W. Yorke reported a case of Indian kala-azar, which was apparently cured with an aromatic diamidine, 4'-diamidino stilbene—R-CH₂CH₂R. The patient was a Hindu aged 31 years, who had been suffering from an irregular fever for 2 or 3 months. He was emaciated with a greatly enlarged liver and spleen. Blood and bone marrow examination showed the presence of Leishman-Donovan bodies, thus confirming the diagnosis. The patient was given 1.0 mg. of the drug per kilo body weight intravenously for 8 days. The total amount injected was 360 mg. The effects of the treatment were not immediately apparent.

but the temperature fell to normal 6 days after the end of treatment. The spleen began to get smaller 10 days afterwards, and it shrunk to normal with great rapidity. At the same time the blood-culture became negative, and 2½ months later the patient left hospital apparently cured.

Adams, A. R. D., and Yorke, W. (1939) *Ann trop Med Parasit* **33**, 323

Kala-Azar in Children

Diagnosis and Treatment

H. Spiropoulos of Athens discussed the diagnosis and treatment of leishmaniasis in children. Kala-azar, as occurring endemically in the Mediterranean countries, usually attacks children and diagnosis can often be difficult on account of the slow development, and often latency, of the anaemia and enlarged liver. The younger the child and the longer the anaemia persists, the more serious should the condition be regarded. Many of these cases are resistant to trivalent antimony treatment and the author found that neostibosan—a pentavalent antimony compound, more effective and less toxic than trivalent antimony—supplemented with vitamin C preparations often cleared up the disease.

Spiropoulos, H. (1939) *Arch Kinderheilk*, **117**, 244

KIDNEY, SURGICAL DISEASES

See also B. E. M. P., Vol. VII, p. 380, Cumulative Supplement, Key Nos. 829-840, Surveys and Abstracts 1939, p. 393, and p. 118 of this volume.

Congenital Abnormalities

Crossed ectopia

J. R. Sutes and J. A. Bowen report a case of crossed ectopia of the kidney. Hunter first recorded the condition in 1785 and since then Townsend and Humkin have tabulated 159 cases; the present authors also note a case reported by Carleton.

According to previous authors, the incidence of ectopia of the kidney is one in 1,000 necropsies, of crossed ectopia, one in 8,000 or one in 6,500. The preponderance is toward the male and toward the right side, and there is usually, but not always, some fusion of the kidney substance. As stated by Carleton, although the factors causing fusion or adhesion between the early kidneys are not clear, such fusion must occur, the kidney mass occupying the most cranial position at the time of the fusion predetermining the side upon which both kidneys ascend to their permanent position.

The symptoms are aching pain, and the presence of a mass, with or without haematuria. Infection and stone have been found but apparently not in any greater proportion than in kidneys in the normal position. Surgical removal of the lower kidney has been found the method of choice; catheter drainage and dilatation of the ureters have not produced satisfactory results.

In Sutes and Bowen's patient, a male aged 37, cystoscopic examination showed a moderately inflamed bladder, with normal ureteral orifices although the right one appeared bulging. The left side was catheterized easily and produced clear urine; the right side was catheterized only after being split with the electrotome; 25 c cm of dark fluid were withdrawn from it and produced a pure culture of *Staph aureus*. From the urogram and 2 pyelograms crossed ectopia was diagnosed.

Treatment. The right catheter was left in situ for 4 days and the pelvis lavaged every 4 hours with solution of 1 in 3,000 merthiolate. On the third day after discharge the patient had an aching sensation in both lower legs which diminished on the left but increased on the right. A diagnosis of bilateral thrombophlebitis of the lower extremities was made. Under treatment the left leg rapidly responded but the right progressed to dry gangrene of the foot and lower third of the leg. A mid-thigh amputation was done; the pathologist reported occlusion of the popliteal artery about 6 inches below the amputation site. The stump healed by first intention and the patient was discharged on the seventeenth post-operative day. The authors remark that it will always be questionable whether or not the

patient's subsequent difficulties may not have been prevented by surgical interference on his first admission

Carleton, A (1937) *J. Anat.*, **71**, 292

Stites, J R and Bowen, J A (1939) *J. Urol.*, **42**, 9

Townsend, T M. and Frumkin, J (1937) *Urol. cutan. Rev.*, **41**, 324.

Polycystic Disease

Unilateral Multilocular Cystic Kidney

W A Dakin records a cystic kidney on the left side, without a renal pelvis, ureter, or any vascular pedicle, in a female child, aged 2 years, in whom the mass had been palpable from birth. This cystic mass, taking the place of the left kidney, consisted of 10 large intercommunicating loculi and numerous smaller ones from 1 to 2 cm in diameter. It was successfully removed. This abnormality must have originated extremely early in foetal life, about the 25th day, and before the ureteric bud joins the metanephros, and has very seldom been reported. It is known that congenital anomalies, including complete absence of the kidney, are commoner on the left than on the right side, but renal cysts are rare, in an analysis of 400 patients examined urologically by the author there were 3 examples only. The following classification of cysts in the kidneys is given. (1) bilateral congenital polycystic kidneys, (2) simple cysts (a) small multiple retention cysts, associated with infection and localized obstruction of the tubules only, thought to be usually acquired, (b) large solitary cysts generally unilateral, of which some 250 have been recorded, these are said to be commoner in females than in males, probably acquired, and very rare in children. (3) large multilocular unilateral cysts

Dakin, W A (1940) *Canad. med. Ass. J.*, **42**, 531

Infections

Staphylococcal Infection of Cortex

P J Kahle *et al* reported 11 cases of staphylococcal infection of the renal cortex. Contrary to the usual findings *Staph. aureus* was found to be the causal organism in nearly all the cases. The symptoms of cortical abscess appeared to develop more rapidly, and the febrile reaction appeared to be more marked than in carbuncle. In both conditions pain in the loin was invariably present, but rigidity of the lumbar muscles varied in degree, and was sometimes absent. The leucocyte count was generally higher in carbuncles and the percentage of polymorphonuclear leucocytes lower in carbuncles than in cortical abscess. Blood culture was not helpful in the diagnosis. Except in one case in which the abscess had ruptured into the calyx, the urine was consistently negative for abnormalities, and culture of the urine from the kidney and bladder generally showed no growth. Cystoscopy showed no changes in the bladder mucosa, and X-rays and pyelography gave no information in about 50 per cent of the cases. Treatment of abscess and carbuncle of the kidney is essentially surgical, a lower mortality seems generally to follow nephrectomy, but excellent results can be obtained by conservative measures in properly-selected cases.

Kahle, P. J., Green, M M., and Tomskey, G. (1940) *J. Urol.*, **43**, 774.

Renal Infarction

F A B Sheppard records a case of this rare condition in an Indian male, aged 24, who was suddenly attacked by severe pain in the left loin, with vomiting 6 times. The urine was normal and, radiologically, no evidence of a renal lesion was seen. At operation, a week after the onset, under spinal anaesthesia, a lumbar incision showed a slightly enlarged left kidney, soft and nearly purple in colour, and the branches of the renal artery did not pulsate. The renal artery and vein contained blood clot. There was not any explanation of the thrombosis.

Sheppard, F A B (1940) *Brit. J. Surg.*, **27**, 603.

Hydronephrosis

Treatment

G Marion recommends conservative treatment in cases of large hydronephrosis, i.e. when the renal pelvis contains from 100 c cm to 1 litre of fluid. His method

consists of removal of the obstruction, high suspension of the kidney, and drainage by nephrostomy. The drain is removed when pyelography indicates that the renal pelvis has shrunk as much as possible. A remarkable degree of restoration of renal function and prolongation of life is said to be possible with such conservative treatment. Nephrectomy should be considered as a last resort. Two cases are described, one being that of a young man with a large hydronephrosis of congenital origin, and the other an infected hydronephrosis due to ureteral calculus. In these cases the function of the kidney was markedly improved.

Marion, G (1939) *J Urol méd chir*, **48**, 5

Tuberculosis

Clinical Significance of Tubercle Bacilli in Urine

C. E. Dukes compared the urine in tuberculous bacilluria and in urinary tuberculosis when tubercle bacilli in the urine are accompanied by tuberculous lesions in the urinary tract. A healthy kidney cannot excrete tubercle bacilli. Dukes stated that tuberculous bacilluria was commonly due to small tuberculous foci in the kidneys which were unassociated with symptoms and rapidly healed up. They are more likely to be found in association with blood-borne infection such as occur in tuberculous disease of the bones and joints. The bacilli are present intermittently in small numbers in the urine and cannot as a rule be detected with the microscope. They can be demonstrated by injecting a guinea-pig. In urinary tuberculosis the urine contains many pus cells and the organisms can be found in stained films. The urine is often turbid, it is clear in tuberculous bacilluria, and the excretion of organisms is constant and continues until the tuberculous lesion is healed.

Differential Diagnosis

Sterile pyuria—T. Moore pointed out that the older belief that sterile pyuria means urinary tuberculosis has more recently been modified. There are non-tuberculous cases of abacterial pyuria, one group of which is probably caused by a filtrable virus. This condition is of importance since a diagnosis of urinary tuberculosis may be made and, when only one kidney pelvis is involved, nephrectomy may be carried out. The most important step in diagnosis is careful examination of the urine for bacilli, and guinea-pig inoculation. The absence of any destructive renal changes on excretion urography, and the fact that on cystoscopy inflammatory changes are not particularly marked round the ureteric orifice as in tuberculosis, render the diagnosis relatively easy. In cases of doubt the therapeutic test, namely the intravenous administration of 0.3 g. neoarsphenamine weekly for 4 weeks, is a valuable aid. The condition, which is resistant to all ordinary forms of treatment, clears up in a remarkable manner with this treatment.

Dukes, C. F. (1939) *Brit med J*, **2**, 799

Moore, T. (1940) *Brit. med J*, **1**, 170

Tumours

Wilms's Tumour

I. I. Kaplan and M. F. Campbell report a case of Wilms's tumour in a male child of 11 months which was treated by a combination of surgery and X-rays. Immediate operation being deemed inadvisable, X-irradiation was given to the anterior, posterior, and lateral areas in the hope of reducing the tumour mass which filled the greater part of the left upper abdomen. A dose of 1,200 r. was given to each area, the factors used being 200 kilovolt, 1 mm. copper plus 1 mm. aluminium filtration, at 50 cm. distance, 200 r. per treatment at daily intervals to alternate areas. The size of the tumour was thus markedly reduced, and 2 months later a well-encapsulated Wilms's tumour and the right kidney were removed. Following the operation an additional 800 r. were given over the anterior and posterior abdomen. Further courses of irradiation were given at intervals and the child was free from symptoms of recognizable recurrence or metastasis, and had grown normally 3½ years later, a noteworthy result in the light of the rarity of successful results in this condition.

Familial Tendency

P. Nowlin reported the cases of 2 brothers, each of whom died from malignant disease of the kidney, and who had a family history that strongly suggested that the death of a sister was from the same cause. The author pointed out that a familial tendency to renal malignant disease appeared to be unusual, since he had found no indication of this in a comprehensive review of the literature.

Kaplan, I. I., and Campbell, M. F. (1939) *Arch. Pediat.*, **56**, 766.
Nowlin, P. (1940) *J. Urol.*, **43**, 654.

Calculi*Aetiology*

Influence of diet.—H. Schneider and H. Steenbock summarize the influence of diet upon the formation of urinary calculi. Thus vitamin-A deficiency and an excess of calcium over phosphorus have both been shown to play a part. By feeding rats upon a diet deficient in phosphorus, the authors produced calcium citrate calculi. It was shown that the low phosphorus intake increased the urinary citric acid excretion. This may be due to increased alkalinity in the tissues. Owing to the difficulty of detecting citrates in ordinary laboratory analysis, the authors thought that these stones may be more common clinically than is usually supposed.

Calcium excretion.—R. H. Flocks had previously shown that increased urinary calcium excretion played a very significant part in the pathogenesis of calcium calculi, because high calcium excretion was associated with approximately 66 per cent of cases of calcium urolithiasis and because, in all patients with recurrent stones, or rapidly growing stones, high urinary calcium excretion was present. Moreover, among patients with calcium urolithiasis there was a large group of individuals with a high urinary calcium excretion without any bone disease, evidence of hyperparathyroidism, change in blood calcium or phosphorus, or other demonstrable abnormality of calcium metabolism. The present paper shows that, in the normal individual, the factors causing variations in urinary calcium were the intake of calcium and phosphorus, the acidity of the ash of the diet, and the intake of vitamin D. The pathological conditions effecting changes in urinary output of calcium are marked immobilization, intrinsic bone disease, changes in endocrines—the parathyroid, thyroid, and pituitary—certain intrinsic renal changes and certain intrinsic changes in individuals. The management of calcium urolithiasis from the view-point of calcium metabolism comprised the prophylaxis and management of patients with calcium urolithiasis and a high urinary calcium, and the management of patients with calcium urolithiasis and a normal or low urinary calcium.

Alkali therapy.—H. L. Kretschmer and R. C. Brown report on the influence of alkalis, used in the treatment of peptic ulcer, on the formation of renal calculi. Among 680 cases of peptic ulcer there were 23 in which renal calculi antedated the ulcer treatment, and 33 in which the alkaline treatment for ulcer preceded evidence of calculi; the difference, 1.8 per cent, in this series is all that could possibly be due to the use of alkalis. In 1,260 cases of renal and ureteral calculi 7 cases of stone and peptic ulcer were diagnosed simultaneously, in 26 of the patients there was a history of peptic ulcer, but only 15 of them had received alkaline treatment; in 3 of these the stones occurred many years after the treatment for ulcer was discontinued. The conclusion reached is that the alkaline treatment of peptic ulcers has little bearing on the aetiology of renal calculi.

C. W. Eisele found that, in a series of 505 patients with renal or ureteral calculi, 43 (8.5 per cent) had previously had peptic ulcers, and had been treated with alkalis. Another 13 (2.6 per cent) had chronic gastro-intestinal disorders for which they habitually took alkalis. Thus, in 56 patients the ingestion of alkalis must be considered of aetiological importance in the occurrence of urinary calculi. The hyperexcretory calculus in these patients indicates a potential danger of alkali therapy of peptic ulcer.

Hypovitaminosis A.—H. Long and L. N. Pyrah investigated by means of the photometer method the vitamin-A reserves of 25 patients who had suffered from renal calculus. A similar examination of 65 control cases was made. There was a definite sub-normal dark adaptation in 40 per cent of the calculus cases, but no

such definite subnormality in the controls. Furthermore, while 75 per cent of the control cases showed normal dark-adaptation, only 36 to 40 per cent of the calculus cases were normal. Vitamin A in daily doses of 13,000 units over 4 to 5 weeks effected no gross improvement in the results of the photometer test in patients suffering from renal calculi. The figures are not sufficiently striking to allow of the conclusion that deficiency of vitamin A is at most more than a contributory factor in the complex aetiology of urinary calculi.

Sulphapyridine.—N. Plummer and I. McLellan reported 2 cases of renal calculi which followed treatment with sulphapyridine. It has been established that the haematuria which sometimes accompanies sulphapyridine medication is due to the formation of its crystals in the urine. These crystals may form, or form the basis of, renal calculi. The first patient received a total of 555 g. of the drug in the treatment of subacute bacterial endocarditis which ultimately proved fatal. The second patient was suffering from pneumonia and received only 11 g. of the drug. Haematuria was present in both cases and one had renal colic. Serial X-rays in the second case revealed the calculi which were later dissolved or washed out. The authors suggested that frequent urinary examination should be made during the giving of sulphapyridine and if haematuria occurs the drug should be stopped.

W. Antopol reports that in 16 out of 40 patients treated with sulphapyridine the urine contained red cells when examined microscopically. In one case necropsy showed absence of calculi in the urinary tract, although a haemorrhagic papillitis and pyelitis were present. Accompanying the haematuria there was typical ureteral colic which disappeared promptly after discontinuance of the sulphapyridine treatment. One patient had anuria 2 days after sulphapyridine therapy was begun, but when discharged from hospital, was free from residual symptoms.

Sulphathiazole therapy. P. Gross *et al.* found that the administration of sulphathiazole, 2-(*p*-aminobenzene sulphonamido)thiazole, or of sulphamethylthiazole, 2-(*p*-aminobenzene sulphonamido)-4-methylthiazole, both of which drugs possess high anti-pneumococcal and anti-streptococcal activity, produced urolithiasis in rats. The sulphathiazole uroliths contained 4.2 per cent free, and 25 per cent conjugated, drug; the sulphamethylthiazole uroliths contained 29 per cent free, and 56 per cent conjugated, drug. Both contained water-insoluble material comprised partly of lipid. The incidence of urolithiasis from these two drugs was less than that from sulphapyridine, and, like the latter, was associated with secondary infection and pyelonephritis which occasionally caused death. The uroliths caused by these drugs, like those caused by sulphapyridine, are capable of spontaneous solution and disappearance. A considerable proportion of the uroliths deposit in the renal tubules, they sometimes cause urinary block. The authors suggested the term 'urolithiasis medicamentosa' for the condition in which the administration of drugs is followed by their deposition in the free or conjugated form in the kidneys or urinary passages.

A. F. Knoll and F. B. Cooper reported a case of haematuria following the administration of sulphathiazole. The haematuria disappeared 4 days after the discontinuance of the drug, and was associated with a rise in blood-pressure and with a high blood non-protein nitrogen. It had been shown experimentally that uroliths from this drug were deposited to a considerable degree in the renal collecting tubules, whereas sulphapyridine uroliths were generally found in the extra-renal urinary passages. Such uroliths may dissolve spontaneously on discontinuance of the drug. The advisability of attaining excessive high concentrations of such relatively insoluble substances as sulphapyridine and the thiazoles appears to be questionable, because of the correspondingly increased chances of urolithiasis. Dehydration may also produce excessively high blood-concentrations of these drugs with similar sequelae.

Clinical Picture

J. A. Hyams and H. R. Kenyon writing on the not infrequent latency of symptoms characteristic of urinary calculi, and the resulting failure of recognition, report cases in which investigation of patients with minor symptoms led to the discovery of all grades of stone formation. Since many calculi are present long before detection, they are, when found, large and accompanied by advanced changes in the kidney.

A history of previous calculus with persistent infection of the urinary tract by urea-splitting bacteria, in spite of intensive treatment, necessitates frequent urographical examination

Prognosis

Factors in recurrence - C. C. Higgins discusses the factors responsible for the recurrence of renal calculi. Infected urine accounts for many recurrences, although stones often reform in the presence of sterile urine. Septic foci have been held to favour recurrence by some authors. Another undoubted factor is stasis, often due to a ureteric stricture. Vitamin-A deficiency, hyperparathyroidism, and metabolic abnormalities, such as cystinuria, play a part. Trauma during the first removal of a stone appears to account for some recurrences, and pelvolithotomy is therefore a better operation than nephrolithotomy. In every case of renal calculus it is important to ascertain whether any of these factors are present. If they are they should be dealt with to prevent the recurrence of the stone.

Diagnosis

Insulin-free pancreatic extract - J. A. Lazarus employed an insulin-free pancreatic extract as an aid in the cystoscopic treatment of impacted ureteric calculi and in spastic occlusion of the ureter. During the past 3 years he has treated more than 100 cases of ureteral occlusion due to calculus, spasm, and stricture, with uniformly good results. An important fact noted in using the extract was that cystoscopy had to be performed within 5 minutes after its administration, since its maximal effect generally occurred within this limit. In cases in which the cystoscopic manipulation required more time than that, it was advisable to administer the preparation after the cystoscope was introduced. The dose employed was 1 c.c., given into the gluteal muscles. In a few stubborn cases a second dose was required to obtain the desired results. In no cases were there any untoward symptoms noted.

Pneumopyelography - G. Bravetta reported the use of retrograde injection of air or gas into urinary passages to demonstrate the presence of calculi. The contraindications to the method are uraemia, pyrexia, and haematuria. Some calculi, e.g. those composed of cystine or xanthine, are not shown up by uroselectan as they are transparent, but they can be made visible by injection of air into the ureters. The method must be used with care but in expert hands it should give good results.

Treatment

Operative A-ray control - G. D. Oppenheimer considers that, whereas some of the quite frequent recurrences of renal calculi after operation for their removal are true recurrences, many are due to a residual stone left in the kidney. Calculi or their fragments sometimes cannot be felt, and X-rays can be used at the time of operation to disclose them. After all stones have apparently been removed from the kidney and renal pelvis, the kidney should be X-rayed, the film rapidly developed and, if any further stones are shown, these should if possible be removed. In 85 such examinations, 29 showed calculi or fragments which could not be felt. There are some disadvantages to this method, such as lengthening of the operative procedure, but they do not outweigh its value in the prevention of residual calculi.

Prophylaxis - W. M. Kearns discussed the prevention of recurrence of urinary calculi. A fundamental requirement for prophylaxis is the administration of vitamin A, with other vitamins for their synergistic action. In a group of 164 patients, during 13 years, who adhered to such a dietary, there were recurrences only in 8 cases (4.8 per cent). A water intake of 60 ounces daily was recommended in order to promote mechanical flushing and to ensure adequate water for solution of urinary solids.

Transurethral manipulation - G. J. Thompson and J. M. Kibler discuss the treatment of ureteral calculus. Although many patients pass the stones spontaneously, they are usually small. The authors treated 361 cases by transurethral manipulation. The ureter must be readily accessible for this manoeuvre, for example, it cannot be done in the presence of an enlarged prostate. It is advisable to allow the stone to descend to the lower third of the ureter before an attempt is

made to perform this manipulation. Uretero-lithotomy may be preferable to waiting for the stone to assume a favourable position. Whether transurethral manipulation is done with multiple catheters or one of the various extractors, it is only suitable for in-patient work. The authors operated under direct vision through a Braasch cystoscope. After operation a catheter was left in for from 48 to 72 hours to prevent obstruction from any oedema of the ureter that may occur. X-ray examination is also made so that the patient may see that the original stone has been removed if another should form.

Out of the 361 cases, 91.4 per cent were successfully treated, in 1.1 per cent the treatment failed, in 7.5 per cent uretero-lithotomy was successfully performed after the attempted manipulation. Mild pyrexial reactions occurred in 8.8 per cent of the cases. Severe complications, such as pyelonephritis and thrombophlebitis, were extremely rare and all the patients recovered. The operation must be very gently done if complications are to be avoided. Only a few days in hospital are usually necessary. Renal function may have been inhibited by the impacted stone, but returns soon after the calculus is removed.

Antopol, W. (1940) *J. Urol.*, **43**, 589.

Bravetta, G. (1939) *Arch. ital. Urologia*, **16**, 188.

Fisele, C. W. (1940) *J. Amer. med. Ass.*, **114**, 2363.

Flocks, R. H. (1940) *J. Urol.*, **43**, 214.

Gross, P., Cooper, F. B., and Scott, R. L. (1940) *Urol. cutan. Rev.*, **44**, 205.

Higgins, C. C. (1939) *J. Amer. med. Ass.*, **113**, 1460.

Hyams, J. A., and Kenyon, H. R. (1940) *Urol. cutan. Rev.*, **44**, 230.

Kearns, W. M. (1940) *J. Urol.*, **43**, 598.

Knoll, A. F., and Cooper, F. B. (1940) *Urol. cutan. Rev.*, **44**, 292.

Kretschmer, H. L., and Brown, R. C. (1939) *J. Amer. med. Ass.*, **113**, 1471.

Lazarus, I. A. (1940) *J. Urol.*, **43**, 102.

Long, H., and Pritch, L. N. (1939) *Brit. J. Urol.*, **11**, 216.

Oppenheimer, G. D. (1940) *J. Urol.*, **43**, 253.

Plummer, N., and McEllan, F. (1940) *J. Amer. med. Ass.*, **114**, 943.

Schneider, H., and Steenbock, H. (1940) *J. Urol.*, **43**, 339.

Thompson, G. J., and Kibler, J. M. (1940) *J. Amer. med. Ass.*, **114**, 6.

Ureteral Calculi

Treatment

Prostigmin. V. J. O'Connor reported on the use of prostigmin methylsulphate to assist the passage of ureteral calculi. The dosage was 1.0 c.cm. of a 1 in 2,000 solution (0.5 mg. prostigmin), injected subcutaneously, at 3 to 4 hourly intervals, for 4 doses. In 6 patients who had suffered for months from large calculi, the injections were soon followed by expulsion of the stones into the bladder whence they had to be removed in 4 cases. In 12 cases in which attempts had been made to remove ureteral stones by ureteral meatotomy, ureteral dilatation, etc., rapid downward progress and expulsion occurred after prostigmin injections. The author considers that prostigmin injections are worthy of trial in cases in which the lower ureter is not abnormally obstructed.

O'Connor, V. J. (1939) *Brit. J. Urol.*, **11**, 325.

Bilateral Ureteral Blockage

Following Sulphonamide Therapy

That a considerable proportion of the sulphapyridine ingested is excreted in the urine as the insoluble mono-acetyl derivative and that the latter may crystallize out with the formation of renal calculi is recognized. The occurrence of gross or microscopic haematuria associated with the presence of acetylsulphapyridine crystals in the urine is a not uncommon complication of sulphapyridine therapy, and some of the cases of haematuria may go on to anuria with nitrogen retention.

and even death. F. Smith *et al.* reported a case in which, following the administration of 42 g. of sulphapyridine and 9 g. of sulphanilamide over a period of 4 weeks, there occurred anuria due to complete blockage of both ureters with acetylsulphapyridine crystals. Bilateral pyelotomy, decapsulation, and retrograde ureteral dilatation was performed, following which the patient made a complete recovery; the blood-pressure, which six hours before operation was 196/95 mm. Hg, returned to normal within 3 days. The authors believed that the formation of calculi during sulphonamide therapy is probably due to idiosyncrasy, but that one of the factors which tends to increase the likelihood of this complication is reduction of fluid intake either voluntary or due to uncontrolled vomiting. The practice of giving sodium bicarbonate with sulphonamide drugs does not seem to have any prophylactic effect. If haematuria, renal colic, or oliguria occur the drug should be discontinued at once and fluids given intravenously.

Smith, F., Evelyn, K. A., and Nolan, J. F. (1940) *Canad. med. Ass. J.*, **42**, 27

Diagnosis

The Delayed Urogram

W. I. Braasch and A. K. Doss reviewed the clinical significance of the delayed urogram. A plain X-ray was made of the urinary tract followed by the injection of 6 to 8 c.c. of a pyelographic medium (a 20 per cent solution of hippuran) through a catheter into the renal pelvis. The patient remained in the dorsal decubitus position, and X-ray exposures were made after 10 to 15 minutes and repeated as often as was indicated by the rate of expulsion of the medium. If the medium had disappeared after 15 minutes, it was of no clinical significance. Many factors were found to influence the rate of drainage from the pelvis and ureter. Stasis in the pelvis or ureter might be caused by obstruction or a physiological impediment to excretion. Interference with the nerve supply and fibrosis from chronic infection would produce the latter. Repeated overdistention with bougies would also produce this type of stasis in the ureter. The two types of stasis might be differentiated in that obstruction caused pain, and it was usually absent when there was no obstruction. The delayed urogram is useful in determining whether a doubtful obstruction is present and, unless this evidence of stasis is seen in these cases, operation is not justifiable.

Braasch, W. F., and Doss, A. K. (1939) *Proc. Mayo Clin.*, **14**, 712

Operations

Unilateral Nephrectomy

Reserve capacity and compensatory hypertrophy in removing kidney.—H. G. Hanley investigated the reserve capacity of the kidney and of the compensatory hypertrophy produced by the removal of one kidney, in a group of 213 cases comprising hydro-nephrosis, pyonephrosis, calculus, tuberculosis, neoplasms, and chronic nephritis. A striking fact was the high operative mortality, 10.7 per cent, which was largely due to 9 deaths in the pyonephrosis group and 6 in the neoplasm group. Of the 182 patients traced, a further 37 died after leaving hospital, bringing the total mortality up to 28 per cent; of these 37 late deaths, 34 occurred within 2 years of operation and were mostly from renal failure. Two other patients, both suffering from renal tuberculosis, lived 4 and 5 years respectively. In the neoplasm group 11 late deaths occurred in 2 years, but an encouraging fact was that 8 patients were alive and well 2, 3, 6, 7, 8, 8, 10 and 11 years respectively after operation; of the 5 patients whose kidneys after removal showed evidence of chronic nephritis, one died 8 days after operation and the others within 8 months; in none of them was there anything to indicate the true nature of the pathology before operation. From the clinical aspect 3 per cent of the patients still had symptoms severe enough to cause inconvenience, 60 per cent had a renal function below normal, while 11 were definitely ill and exhibiting signs of renal failure. Of 122 living patients, 62 said that they felt perfectly well. No relation could be established between the sex or age of the patients and the ultimate prognosis or renal efficiency to be expected after

a nephrectomy. The author held that a Van Slyke clearance test consistently below normal should negative any radical surgery, whatever the blood-urea figure might be. Radiographic examinations to the remaining kidney before and after removal of its fellow definitely proved the presence of compensatory hypertrophy in some, but not all, cases. Compensatory hypertrophy is not confined to young patients, one case in this series being 53 years of age. Pain did not always accompany hypertrophy. In some cases a pelvic type of hydronephrosis occurred in the remaining kidney. The author concluded that, though at present nephrectomy is the only available treatment for certain renal conditions, the high mortality and persistence of symptoms in many cases calls for continued search for more conservative measures, particularly in hydronephrosis and calculi.

Hanley, H. G. (1940) *Brit. J. Surg.*, **27**, 553.

LABOUR · NORMAL

See also B. L. M. P., Vol. VII, p. 417, and Cumulative Supplement, Key Nos. 841-844.

Incidence of Day and Night Deliveries

V. Spiller investigated the relative frequency of deliveries by day to those by night in 2,225 deliveries during 1934-7 at the Royal Free Hospital, London. Reckoning night as from 8 p.m. to 8 a.m. there were 1,084 day births and 1,141 night births, or 5.25 per cent more births by night than by day. With regard to primiparae, only 0.9 per cent more are delivered by night than by day, whereas the corresponding figure for multiparae is 22 per cent. Other estimates of the occurrence of delivery have defined night variously as 7 p.m. to 7 a.m. and 10 p.m. to 10 a.m. Spiller considers that the variations of his estimates are well within the limits of probable error, and suggests a comparatively even distribution of births over the 24 hours.

Spiller, V. (1940) *Brit. med. J.*, **1**, 435.

Phenomena of Normal Labour

Causes of Onset of Labour

Acetylcholine. —F. Navratil reports investigations of the action of acetylcholine found in the placenta on the course of labour. The placenta has a very high acetylcholine content and detailed examinations by many research workers, together with the author's experiments, have shown that choline plays an important part, being one of the principal factors determining the strength of the periodical uterine contractions constituting the first stage of labour. A sudden increase of the acetylcholine level in the placenta is probably the initial factor determining the onset of pains and therefore acetylcholine can be regarded as the principle which, after attaining a certain level in the placenta, initiates labour. The most important therapeutic deduction is the use of acetylcholine in insufficient contractions and in uterine atonia, as corroborated by Bell and Playfair.

Stages of Labour

Salt-poor diet for lessening pains and duration. —F. E. Wadlow stated that most procedures for lessening the pains and length of labour are dangerous except in expert hands. He gave a salt-poor diet to 70 women in the last weeks of pregnancy to obtain this end. The results were very good and no harmful effects were noted. There were no foetal or maternal deaths in the series, although 13 of the labours were abnormal. The salt-poor diet acts because in the last few months of pregnancy water is retained in the body, probably through action of the pituitary. This retention leads to oedema of the uterine musculature and the cervix. The oedema causes the contractions to exert less effect than they would on non-oedematous tissue, and the cervix dilates more slowly. The salt-poor diet leads to expulsion of this water and the labour is shortened. A salt-poor diet also lessens the excitability of the nervous system, as in some epileptics. This is thought to be the explanation of the decrease in pain.

Rupture of Membranes

Test for rupture of membranes. J. Irving Kushner described a test for establishing whether or not the membranes have ruptured during labour. The pH of the vaginal secretion usually varies from 4.5 to 5.5, if amniotic fluid is added to it, it becomes more alkaline, and the pH rises from 7.0 to 7.5. Two tests were carried out on a series of 50 patients. In the first test a sterile cotton-tipped applicator was inserted deeply into the vagina, a strip of nitrazine paper was touched with it, and the paper was compared with a pH colour chart. In the second test a sterile applicator soaked in an 0.2 per cent alcoholic solution of bromothymol blue was inserted deeply into the vagina and if on withdrawal it had turned green the membranes had ruptured. The first test gave the more accurate results. In the 50 cases the first test was correct in 97 per cent of cases and the second test in 74 per cent. In 8 patients admitted with a history of ruptured membranes, the first test was correct in 75 per cent and the second test in only 50 per cent. The same results were obtained in 7 patients admitted with an unknown history. The nitrazine test is therefore very useful in those with a history of possible rupture of the membranes when it cannot be confirmed by clinical examination.

Kushner, J. I. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 1046

Navratil, E. (1939) *Zbl. Gynak.*, **63**, 1883

Wadlow, E. F. (1940) *Amer. J. Obstet. Gynaec.* **39**, 749

Factors in Labour*The Passages*

Role of cervix. F. L. Good, investigating the role of the cervix in pregnancy and labour, claimed to have furnished proof that what has been called the lower uterine segment is only the normal cervix before the onset of pregnancy. The cervix is really taken up and, as a part of this process, a ring is formed, this ring is a perfectly normal physiological phenomenon, and has a distinct function in the process of labour. The taking up of the cervix starts in early pregnancy, and continues even through labour. Within a few hours after the end of labour, the cervix is 'taken down' and begins to resume its normal condition. The author claimed that, since the lower uterine segment is simply what was the cervix before conception, many present-day obstetrical principles should be altered. He suggested dividing the stages of labour into 5, instead of the usual 3, namely (1) taking up of the cervix; (2) from the beginning of dilatation of the external os to its full dilatation; (3) from full dilatation of the external os till birth; (4) from birth to expulsion of the placenta; and (5) from expulsion of the placenta to the time when the cervical cavity has become completely obliterated, and a normal cervix has been formed, a matter of only a few hours.

Good, F. L. (1939) *New Engl. J. Med.*, **221**, 219.

Effect of Stilboestrol on Uterine Contractions

J. H. Peel investigated the effect of stilboestrol on the control of uterine contractility and compared it with that of the natural oestrogenic hormone, oestrone. To 52 unselected pregnant patients he gave a total dose of 10 to 50 mg. in the last 2 to 3 weeks of pregnancy. In many cases contraction of the uterus increased during this time. Of the patients 24 went into labour between the 270th and 280th day of pregnancy, and 29 continued after the 280th day, the longest period of gestation being 289 days. These results show that stilboestrol did not lessen the incidence of post-maturity. The drug, however, shortened the average duration of labour in both primiparae and multiparae. The incidence of forceps delivery was unaltered. In one case primary inertia occurred, but the patient received only a small dose of stilboestrol because her labour began 11 days before it was expected.

In 16 cases stilboestrol was used to induce labour. In 3 cases the foetus was dead, but in the remaining 13 the pregnancy was full term or thereabouts. Ten mg. was given intramuscularly, then a 1 mg. tablet hourly for 10 to 12 doses. In 6 cases only was the treatment successful. Eleven cases of inertia were treated with stilboestrol, 4 with complete success, 3 were partial successes only, as forceps had to be used in 2 of them and the labour lasted for 36 hours in the third, 4 were failures.

Peel concluded that the results in these cases receiving stilboestrol were as good as those in which the natural oestrogenic hormone has been used

Peel, J. H. (1939) *Proc. R. Soc. Med.*, **32**, 1230

LABOUR: BREECH PRESENTATION

See also B. E. M. P., Vol. VII, p. 470

Aetiology

C. K. Vartan analysed 969 cases of breech delivery in an attempt to find the cause of the condition. That the foetus often undergoes spontaneous cephalic version has been noted in all obstetric departments. As term approaches the breech presentation becomes more and more rare. This analysis suggested that the failure to undergo this version is the cause of breech presentations, the commonest cause by far of this failure being extension of the legs. The presence of another foetus in the uterus may also prevent cephalic version in many cases. Such conditions as hydramnios, placenta praevia, contracted pelvis, and pelvic tumours may be considered negligible as aetiological factors of breech presentations.

Vartan, C. K. (1940) *Lancet*, **1**, 595.

LABOUR: OBSTRUCTIONS IN THE SOFT PASSAGES

See also B. E. M. P., Vol. VII, p. 511, and Surveys and Abstracts 1939, p. 394

Obstruction in the Vagina and Vulva

Dermoid Cyst of the Vagina

H. W. Johnston records a pedunculated dermoid cyst which did not give rise to any symptoms and was first detected during the second labour, when it appeared at the vagina before the head of the child, the passage of which it did not obstruct. After delivery it was found to arise from the anterior wall of the vagina at the junction with the cervix, and was attached by a very fine longish pedicle, it was easily removed. Its widest diameter was 4 inches. It contained thick sebaceous material and matted hair. Reference is made to 3 other recorded cases (Cullen, Bland Sutton; Curtis).

Bland Sutton, J. (1917) *Tumours Innocent and Malignant*, London, 6th ed., p. 527.

Cullen, T. (1905) *Johns Hopk. Hosp. Bull.*, **16**, 207.

Curtis, A. H. (1913) *Surg. Gynec. Obstet.*, **16**, 715.

Johnston, H. W. (1939) *Canad. med. Ass. J.*, **41**, 386.

LABOUR: COMPLICATIONS OF THE THIRD STAGE

See also B. E. M. P., Vol. VII, p. 523; and Surveys and Abstracts 1939, p. 395

Inversion of Uterus

Treatment

Adrenaline hydrochloride.—A. F. Daro *et al.* reported 3 cases of acute puerperal inversion of the uterus treated with adrenaline hydrochloride. The drug relaxes the uterine muscle even in the presence of ergotamine tartrate or posterior pituitary solution. This enables the inversion to be reduced. The condition is accompanied by profound shock, which should be treated before any attempt at reduction is made. In all 3 cases the uterus became soft and could be replaced as soon as 10 to 15 minims of adrenaline hydrochloride solution had been given. In 2 cases the position was so desperate that the adrenaline was given while shock treatment was in progress. All 3 patients made a very good recovery. The 15-minim dose can be repeated if necessary, and, if the first dose is given promptly, it may be possible to reduce the inversion before shock occurs.

Daro, A. F., Heskett, B. F., and Schiller, H. A. (1940) *J. Amer. med. Ass.*, **114**, 649.

LABOUR: OPERATIVE AND MANIPULATIVE PROCEDURES

See also B. I. M. P., Vol. VII, p. 533, and Surveys and Abstracts 1939, p. 395

Induction of Labour

Methods

Rupture of membranes -- J. R. McCord induced labour in 322 women by rupturing the membranes. Eighty-seven per cent of the women were induced for hypertension of one kind or another. If the patient had eclampsia every attempt was made to control the convulsions before inducing labour. Most of the patients received quinine and castor oil as well as having the membranes ruptured. If labour did not start 8 hours after the membranes had ruptured, 2 minims of pituitary extract was given and repeated every 30 minutes until labour started. No more than 6 doses were given. In 86 per cent of the labours the latent period was less than 24 hours. If it is longer there is no cause for anxiety unless the temperature rises. Only 47 women in this series experienced a rise of temperature, probably because metaphen was instilled into the vagina at the time of rupture and every 24 hours until the end of labour, where it acted as an antiseptic. 94.7 per cent of the labours took place without complication. The mortality-rate for full-term babies was 4.9 per cent, though these deaths were caused rather by the indications for induction than by the induction itself. Most of the labours were short and the deliveries spontaneous. Examination with the ophthalmoscope in 231 of these women showed typical fundus changes.

Ergot -- C. J. Ehrenberg *et al.* induced labour in 184 patients with small doses of ergot. The drug was given in the form of the dried powder, in doses of 12 grains by mouth every 2 to 3 hours. From 1 to 2 fluid ounces of castor oil was given half an hour before the first dose of ergot. Two doses of ergot were usually sufficient to produce uterine contractions within 24 hours of the first dose. If labour began after 1 dose the treatment was stopped. Although 17 of the patients suffered from toxæmia of pregnancy, there were no maternal deaths in this series and no increase in maternal morbidity. There were 3 foetal deaths. Ehrenberg *et al.* considered that, contrary to classical teaching, ergot may be given safely and with success during labour provided a standardized preparation which does not deteriorate is used.

Oestrogenic therapy -- S. Lubin and R. Waltman gave oestradiol to 27 multiparae and 9 primiparae in an attempt to induce labour near, at, or beyond term. Intramuscular injections were given, the total dosage ranging from 10,000 to 350,000 I. U. The number of injections varied from 1 to 6, the interval between 2 injections usually being 24 hours. No other aids to induction were used. Of the patients, 8 were probably induced by the hormone. In 4 primiparae shortening of labour could reasonably be attributed to its use. The onset of labour bore no relation to the dose given. The authors concluded that it is possible that oestradiol given near, at, or beyond term may induce labour.

R. K. Kepp reported on the use of oestrogenic hormones for the induction of labour in cases of prolonged pregnancy and of primary weakness of labour pains. In 50 per cent of such cases it had been found that quinine and posterior pituitary extract was effective. In 56 cases of prolonged pregnancy in which cardiazol-quinine and posterior pituitary extract had been given alternately, at intervals of 30 minutes, for 4 doses without effect, this treatment was repeated after a few days together with 50,000 to 200,000 international benzoate units of oestradiol benzoate. The author considered that oestrogenic substance is useful in a proportion of cases of pregnancy, but that it is not possible to foretell in which cases it will prove of value. He also employed oestrogen for primary weakness of labour pains and found that the administration of 50,000 to 100,000 international benzoate units produced a notable improvement in uterine contractions, within 30 minutes, in 15 out of 18 cases. It also sensitized the uterus to respond more readily to quinine and pituitary.

Ehrenberg, C. J., Robbins, O. F., and Haugen, J. A. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 653

- Kepp, R. K. (1939) *Geburtshilfe und Frauenheilkunde*, **1**, 650
 Lubin, S., and Waltman, R. (1949) *Surg. Gynec. Obstet.*, **69**, 155
 McCord, J. R. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 587
 Frank, F. (1907) *Arch. Gynaec.*, **81**, 46
 Latzko, W. (1909) *Wien. klin. Wschr.*, **22**, 477
 Sellheim, H. (1908) *Z. Gynaec.*, **32**, 133
 — (1909) *Beitr. Geburtsh. Gynaec.*, **14**, 88

LABOUR: ANAESTHESIA AND ANALGESIA

See also B.E.M.P., Vol. VII, p. 573, Surveys and Abstracts 1939, p. 396, and p. 19 of this volume

Soluble Evipan per Rectum

G. Rosenblum and A. N. Webb used rectal evipan sodium (hexobarbitone-soluble) as an analgesic agent in the labour of 41 primigravidae and 34 multiparae. Most of the patients received 2 g. of the drug, heavier patients required 3 g., and some required a second dose; 35 per cent of the patients required some supplementary analgesic therapy. The action of the drug varied in different patients. The analgesia was very short, the average period being 2½ hours. Amnesia was complete in some patients and absent in others.

The drug produced localized muscle-twitchings in several patients, as the patients dropped off to sleep they disappeared and they were rarely severe. In 2 cases reported in detail, severe reactions resulted. The patients became cyanosed and shocked with diminution of respiration. Both patients recovered. All the babies were drowsy for about 24 hours and there were 5 cases of asphyxia neonatorum, 2 of which were severe. The authors concluded that the rectal administration of evipan sodium is not suitable for analgesia in obstetric practice.

Rosenblum, G., and Webb, A. N. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 1075

Pentothal Acid

G. C. Steel gave pentothal acid (a thiobarbiturate preparation) to 200 primiparae and multiparae to ease the pains of labour. During the first stage, when the pains began to come every 5 to 7 minutes the patient was given 6 to 8 gr. Three-quarters of an hour later she was given the same dose. From then on she was given 2 to 4 gr. every half-hour or three-quarters of an hour, depending on her response. On delivery the total dose was usually 25 to 35 gr. During the second stage the patient was also given gas and an anaesthesia.

The results in this series were very satisfactory. A co-operative patient was found to be drowsy and sleepy between the pains and to wake up refreshed and undistressed for the passing of the pain. There were 5 still-births in this series in no way applicable to the use of the drug. Most of the babies breathed spontaneously as soon as the head was born. The analgesia obtained was good but the amnesia not very great. However, Steel considered the lack of amnesia of little importance. The duration of the labour was not lengthened, possibly due to increased tonicity of the uterus. The drug was therefore considered to be contra-indicated in trial labour until it is certain that the head will go through and in occipito-posterior cases until the head has rotated. Toxaemia of pregnancy is another contra-indication to the use of pentothal.

Steel, G. C. (1939) *Lancet*, **2**, 251

LARYNX DISEASES

See also B.E.M.P., Vol. VII, p. 612, Cumulative Supplement, Key Nos. 918-927; and Surveys and Abstracts 1939, pp. 90 and 398

Tumours

Cysts

J. B. Erich records successful removal in 3 stages of a large congenital cyst of the larynx from a girl aged 17, who had been hoarse since she had learned to talk. It was lined by stratified columnar epithelium with mucous glands; the cyst contained thin whitish fluid. There was not any definite connexion between the cyst and

the ventricle of the larynx or its appendix. Cysts of the larynx are rare; among 722 benign laryngeal tumours seen at the Mayo Clinic up to 1938 there were 35 cysts only. There are 3 kinds: (i) Mucous cysts, the least rare, may occur in any part of the larynx, but are most often seen about the epiglottis where mucous glands are most numerous. They are lined by columnar or cuboidal epithelium which from intracystic pressure becomes much flattened and eventually disappears. (ii) Haemorrhagic cysts practically always occur on the vocal cords and are ascribed to over-use or improper use of the voice. They are never lined by epithelium. (iii) Congenital cysts are the rarest, only 3 of the 35 cysts were of this kind. They are thought to be due to sequestration of the embryonic cells which form the appendix of the laryngeal ventricle and are always deep in the lateral wall of the larynx and close to the appendix of the laryngeal ventricle. The lining of the cysts resembles the epithelium of the appendix of the ventricle. They bulge into the aryepiglottic fold, often into the piriform fossa, and sometimes into the vallecula. Although of embryonic origin and seen in the newly-born, they may not become apparent until adult life.

Papilloma

Oestrogenic therapy—E. N. Broyles found that, in 5 children, the local application of oestrogenic hormone appeared to have a definitely beneficial effect on multiple laryngeal papillomas. This method of treatment was suggested by the fact that oestrogenic hormone can change the infantile epithelium of the vagina to the adult type, and it is a known fact that papillomas of the larynx tend to stop growing at puberty. Treatment consisted of weekly applications of about 0.1 c.cm. (1,000 I.U.) of oestrogenic hormone in oil to the larynx, through a direct laryngoscope, or by spraying the solution directly into the larynx. After a few weeks in each case the papillomas were much fewer, had ceased spreading, or had disappeared. Removal of any remaining growths was not followed by return.

Broyles, E. N. (1940) *Johns Hopk. Hosp. Bull.*, **46**, 319.

Rich, J. B. (1940) *Proc. Mayo Clin.*, **15**, 44.

LATHYRISM

See also B.E.M.P., Vol. VII, p. 651.

Clinical Picture

R. L. H. Minchin describes a syndrome of upper motor neurone paralysis occurring in South India, chiefly affecting the legs, but sometimes ascending higher; it occurs almost exclusively in males between the ages of 19 and 45. The type of paralysis was a spastic paraplegia of the legs, with marked increase of muscular tone, greatly increased deep reflexes and extensor plantar reflex, and often ankle and patellar clonus. Sensation of the limbs was not affected. A peculiar feature was that, in 12 out of 21 cases, the abdominal reflex was present and normal, and in a similar number of cases, though not always the same ones, the cremasteric reflex was also present, thus resembling Erb's syphilitic paralysis. The following diseases were excluded, disseminated sclerosis, traumatic or granulomatous compression of the spinal cord, compression by calcified vertebral ligaments, syringomyelia, amyotrophic lateral sclerosis, subacute combined degeneration, and syphilitic disease of the spinal cord, thus leaving the diagnosis of some form of 'primary' lateral sclerosis. Although there is not any convincing evidence that the syndrome is due to avitaminosis, this possibility, especially a lack of amino-acids, such as tryptophane, is discussed. The syndrome was regarded as identical with lathyrism, although *L. sativus* did not enter into the diet in South India.

Minchin, R. L. H. (1940) *Brit. med. J.*, **1**, 253.

LEAD POISONING

See also B.E.M.P., Vol. VII, p. 658; Cumulative Supplement, Key No. 931; and Surveys and Abstracts 1939, p. 400.

Aetiology

Following Bismuth Therapy

E. Epstein reported the cases of a painter and smelter worker in whom signs and

symptoms of lead poisoning followed the use of bismuth for the treatment of a syphilitic infection. It has been amply proved that lead is stored in the skeleton, in which location it is believed to be harmless. When the stored metal is mobilized, however, and appears in the circulation, a group of symptoms characteristic of lead poisoning may appear, namely pigmentation of the gums, abdominal cramps, constipation or diarrhoea, peripheral neuritis, anaemia, stippling of the red cells, encephalopathies, and other disorders. It was suggested that bismuth may have replaced the lead stored in the bones, and have led to the mobilization of lead and the development of toxic symptoms. Prophylactic treatment of lead poisoning in those exposed to the influence of the metal was suggested in order to decrease the incidence of untoward reactions following bismuth therapy.

Epstein, E. (1940) *Arch. Derm. Syph.*, N.Y., **41**, 38.

Clinical Picture

In Children

A. Levinson and M. Zeldes report 26 cases of lead poisoning of which 20 occurred in children below the age of 5, and the remainder in the age group between 5 and 14. Five of the cases ended fatally. A characteristic feature in most was the presence of neurological symptoms, and especially of convulsions which are not usually frequent in adults. In 20 out of the 26, metallic deposits were observed radiographically in the shaft of the long-bones. The authors considered that the most effective form of treatment is Shelling's method of administering sodium acid phosphate, in 45 grain doses 3 times a day, combined with a high vitamin-F diet and the subcutaneous injection of 10 mg. of vitamin E every second day. When convulsions were present, 100 to 300 c.c.m. of 5 per cent calcium lactate solution given intravenously, proved effective.

Cerebellar form of saturnine encephalopathy—changes in bones. A. Biemond and S. Van Creveld describe the case of a child, 2 years old, poisoned by drinking water contaminated by lead, and the neurological symptoms, namely horizontal nystagmus, tremor of the head and trunk, inability to stand without help, and an ataxic gait. An X-ray examination showed that the distal ends of the radii and ulnae, and especially the lower ends of the femora presented a wide line of varying thickness which may be described as a lead line.

Biemond, A., and Van Creveld, S. (1939) *Acta paediatr.*, **27**, 51.

Levinson, A., and Zeldes, M. (1939) *Arch. Pediat.*, **56**, 738.

Shelling, D. H. (1932) *Proc. Soc. exp. Biol.*, N.Y., **30**, 248.

Diagnosis

Lead Content in Normal Blood

J. N. M. Chalmers, investigating the normal lead content of blood in 70 people without any known industrial exposure to lead, showed that this varies from 30 to nearly 90 μg Pb per 100 c.c.m., and found that there was no great difference in the blood-lead levels in hospital patients and in healthy people. Age seemed to have little relation to the blood-lead values. Of 44 lead-workers without symptoms of lead poisoning, blood-lead values ranged from 60 μg (within the author's normal limits) to 192 μg per 100 c.c.m. Of these workers, 23 had blood-lead values over 100 μg per 100 c.c.m. (the critical limiting value according to some authorities) but could not be regarded as cases of lead poisoning. In 34 of these workers there was some slight degree of stippling of the erythrocytes. It appeared that, as in normal people, lead workers have a wide range of blood-lead values, and there is no definite threshold at which symptoms appear. Individual tolerance to lead appears to vary greatly, and it has been shown that the calcium content of the diet also affects the blood-lead level. Raised concentrations of lead in the blood indicate an increased absorption of lead, but by no means constitute definite evidence of plumbism. They provide a useful estimate of the degree of exposure to lead. There is not any close correlation between the duration of exposure to lead and the blood-lead value. The diagnosis of lead poisoning is essentially clinical, although biochemical and haematological tests furnish valuable additional information.

Chalmers, J. N. M. (1940) *Lancet*, **1**, 447.

Treatment

Apple Therapy

I. A. Manville *et al.* investigated the ability of the apple or its constituents to protect animals from the toxic effects of lead and arsenic. Rats, guinea-pigs, and rabbits were fed on diets low in uronic acid and given in addition large doses of lead arsenate. The diets of the rabbits and guinea-pigs were also deficient in calcium and phosphorus. Apple supplement was given to 1 group of animals in the ratio of lead to apple of 0.74 for the rats, 2.5 for the guinea-pigs, and 3.0 for the rabbits. The rabbits, receiving the largest amount of apple, showed no toxicity and none of them died. Decreasing the amount of apple still gave protection, but not so much. Autopsy in the rabbits showed there was more lead in the bones and kidneys but less in the liver of the animals receiving the apple. In the rats, with a ratio of only 0.74, there was some protective effect. Vitamins, calcium, and other food factors are said to protect from the effects of lead. These experiments show, however, that, even in the presence of a low calcium diet, apple will afford a full protection for the animal.

Vitamin C

A. M. Dannenberg *et al.* tried the effect of large doses of ascorbic acid in the treatment of a case of lead poisoning of a child, aged 27 months. Poisoning occurred as a result of an abnormal appetite for eating painted articles. A diagnosis of chronic lead poisoning with 'lead encephalosis' was made. Treatment consisted of the daily administration of 100 mg. of ascorbic acid by mouth in divided doses, and 250 mg. intravenously. In spite of this treatment the condition grew worse. This appeared to contradict the recent claims of Holmes, Campbell, and Amberg concerning the value of ascorbic acid in chronic lead poisoning.

Dannenberg, A. M., Wideman, A. H., and Friedman, P. S. (1940)

J. Amer. med. Ass., **114**, 1439

Holmes, H. N., Campbell, K., and Amberg, F. J. (1939) *J. Lab. clin. Med.*, **24**, 1119

Manville, I. A., Reithal, I. J., Yamada, P. M., Spencer, T. W., and Richardson, J. R. (1940) *J. industr. Hyg.*, **22**, 36.

LEISHMANIASIS, CUTANEOUS

See also B.E.M.P., Vol. VII, p. 664, Cumulative Supplement, Key Nos. 932-934, and Surveys and Abstracts 1939, p. 401

Treatment

Local

Powdered sulphonamides.—F. Akrawi stated that many treatments of oriental sore are unsatisfactory. Paints and ointments probably do not shorten the length of the ulceration which heals spontaneously. Diathermy and electro-cautery leave large unsightly scars, and solid carbon dioxide, the best of these types of treatment, is not always readily available. Antimony, the classical treatment for leishmaniasis, does not give very good results with oriental sore. This led Akrawi to try sulphapyridine and uleron for the condition. This treatment may be tried on all ulcers, but is more successful in those in which the ulceration extends all over the lesion and there is not much induration around it. The drug was finely powdered and applied daily to the sore, after it had been well cleaned with saline. This treatment was continued for 1 month. If the ulcer had not healed by then it was considered unsuccessful. In 48 cases regularly treated, 37.7 per cent healed in 8 to 15 days; 25.0 per cent healed in 16 to 30 days, 20.8 per cent improved, but 16.5 per cent were unimproved by the treatment. This rate of healing is much more rapid than in other forms of treatment. The smears for *Leishmania tropica* rapidly became negative and remained so in the cured cases. The scar produced was a good one,

and not so ugly as that resulting from methods which involve the destruction of tissue. The action of the drug on the sores is not known. It destroys secondary infection and possibly has some action upon *Leishmania tropica in vivo*.

Akrawi, F (1940) *J. trop. Med. (Hvg.)*, **43**, 4

LEPROSY

See also B.E.M.P., Vol. VII, p. 682, Cumulative Supplement, Key No. 935; and Surveys and Abstracts 1939, p. 40

History

Leprosy in Portugal

J S Vieira in a survey found that Portugal, the European country with the highest incidence of leprosy, has among its population of 6½ millions 3,000 lepers entirely without any care or treatment, one village having 200 lepers. The only attempt at segregation is made in Lisbon where those in an advanced stage of the disease are housed in a pavilion of one of the hospitals. In the Middle Ages, Portugal had for that time a very thorough system of segregation with the object of prevention, at that time a prince there was a leper. After the Renaissance these measures fell into abeyance.

Vieira, J S (1939) *Leprosy Rev.*, **10**, 185

Aetiology

Heredity

L. Keil discusses the hereditary factors in leprosy. In the middle of the last century it was thought that leprosy might be a manifestation of an hereditary disease transmitted from one human being to another, but with the convincing evidence of bacteriology and modern epidemiology heredity became relegated to the background, and only recently has the problem of an inherited predisposition been revived. There is much in favour of the suggestion that in leprosy, as in tuberculosis, the infective micro-organism, environment, and heredity stand in reciprocal relation to one another. Research on twins is advocated as an aid to the assessment of the influence of heredity. The possible courses taken by an infection in uniovular and biovular twins are: (i) the disease might pursue a more or less identical course in both twins; (ii) both might contract the disease but the clinical characters be different, and (iii) one of the pair might contract the disease and the other escape. Among 400 patients in the Leprosy Polyclinic at Paramaribo there were 5 pairs of twins, in 2 of which both were leprosy, in 2 neither was leprosy, and in 1 pair 1 was affected.

Resistance

Writing on the allied subject of resistance or immunity of the individual, which is the main factor responsible for the type of leprosy, L. Muir (1939) points out that the great majority of persons are born with a strong natural resistance to this disease and, if infected, usually do not show any definite lesions, or only abortive forms, or those of the milder neural character. A small minority, perhaps 10 per cent, are born with a low natural resistance, so that after slight exposure to infection the more severe lepromatous form of the disease follows. Evidence of this difference at birth depends on observations such as the following. Two members of one family have been subjected to equal chances of infection, one acquires the severe lepromatous form of the disease, whereas the other, who appears to be in poorer general health, either escapes altogether or shows a mild neural lesion only. As in other diseases, the general health of the subject plays an important part in determining the types of leprosy, for example, other diseases, malnutrition, adverse climate and other conditions favour a severe type of leprosy. Young children are more susceptible than are adults. Local leprosy manifestations may supervene on parts previously injured. Acquired resistance may also be systemic or local, even the most

severe lepromatous form may spontaneously die out, and in the tuberculoid skin lesions of the neural form it is common for the disease to die out at the centre while it spreads at the margin

Possible Entry through Alimentary Canal

E. Burnet and H. Jadfard of the Pasteur Institute of Tunis transmitted leprosy from the corpse of a patient to a hamster by the alimentary canal. For 12 days the hamster's food was mixed with material first from the human spleen which was rich in leprosy bacilli, and later from a cutaneous leproma. The hamster died 311 days after the first meal containing leprotic material, and necropsy showed 2 granulomas in the lower lobe of the left lung which, like the spleen, contained leprosy bacilli and cells. This observation, it is concluded, should attract serious attention to the possibility that leprosy in man may be transmitted through the alimentary canal.

Distribution

F. Muir (1940), medical secretary of the British Empire Leprosy Relief Fund, who made a tour in 1939 through Nyasaland, the Rhodesias, South Africa and Basutoland, Nigeria, and Cyprus, found that the control and relief in force in these countries varied. In Nyasaland, Northern Rhodesia, in some parts of which 3 to 4 per cent of the population are said to be infected, and the Belgian Congo, there are small leper settlements mainly in the hands of trained nurses, generally, but not always, with some medical supervision, and leprosy is not regarded as a major problem. In Southern Rhodesia, South Africa and Basutoland leprosy, though less frequent, is taken more seriously. In Cyprus leprosy is regarded as a minor problem, but with a strenuous effort it is hoped to bring the disease under control. In Nigeria there were, a few years ago, 200,000 lepers, now there are probably double that number, and this presents a major problem, the settlements, all on a voluntary basis, are among the largest and most efficient in the world. A study of leprosy throughout the world shows that the severity of type and the frequency do not always correspond, thus in Africa, where up to 4 per cent of the population in some parts may be infected, the great majority are of a very mild form which readily yields to treatment, in the West Fort Leprosy Institution, Pretoria, all the 12 European patients were of the severe type associated with high susceptibility, whereas only a quarter of the native patients admitted during the same period were of the severe type. In Burma more than 1 per cent of the population are infected, and the high percentage of children affected suggests that the disease is spreading. The diminution of leprosy, so common in the fifteenth and sixteenth centuries, has been ascribed to the gradual elimination of the susceptibles, so that the survivors were more immune. Muir, however, states that the chief reason why leprosy does not spread in Great Britain is that the standard of living and hygiene is high, and he adds that the history of leprosy shows that it is a war disease, and that severe and prolonged war, by lowering the standard of living, creates the conditions in which leprosy flourishes.

Burnet, F., and Jadfard, H. (1939) *Bull. Acad. Méd. Paris*, 3me Sér. **122**, 383.

Keil, F. (1939) *Leprosy Rev.*, **10**, 163.

Muir, E. (1939) *Leprosy Rev.*, **10**, 221.

(1940) *Report of the British Empire Leprosy Relief Fund*, 1939, London.

Clinical Picture

Lesions of the Skin

The lesions of the skin due to leprosy, which have given rise to some difficulty, are classified by E. Muir into those characteristic of the lepromatous, those of the neural forms of the disease, and residual lesions. (1) The lepromatous form is characterized by 3 lesions, nodular, diffuse, and macular, bacilli are numerous, especially in thickened and nodular lesions, the lesions are usually symmetrical, the macules are flat, smooth, and without a ringed margin, numerous, closely packed, soon coalesce and leave a mottled appearance; changes of sensation are

slight, difficult to elicit, and there is not any thickening or tenderness of the supplying nerve branches, or anidrosis. The lepromin test is negative. (ii) The neural form shows major and minor tuberculoid lesions, and the macules (leprides) which are raised above the surrounding skin, have a ringed margin, are as a rule few, but may reach a large size and tend to have a depression in the centre. Changes in sensation are prominent, and the nerve branches may be thickened and tender, and there is anidrosis. Except in the reactionary phase of the major tuberculoid, bacilli are usually absent. The major tuberculoid is the most conspicuous lesion, when activated it is red and swollen, and in severe cases becomes ulcerated. The lepromin test is usually positive. (iii) Residual lesions are of 2 kinds. (a) In both lepromatous and neural leprosy there are sensory and trophic lesions of the extremities and especially of the hands and feet. (b) The residual lesions of the skin in the lepromatous type are conspicuous in proportion to the thickness and fibrous tissue formation of the previous lesion. As a rule the residual lesions of the lepromatous and neural forms can be easily referred to their respective types, but in some communities, especially when the climatic and general conditions are unfavourable and depressing, it may be difficult to draw a distinction between the neural and lepromatous lesion.

Mun, F. (1939) *Leprosy Rev.* **10**, 221

Diagnosis

Potassium Iodide Test

Some years ago B. Moiser tried the potassium iodide test in cases of leprosy that were bacteriologically negative and awaiting discharge as arrested; this trial was, almost from the start, attended by disaster, and was given up. Recently, on the advice of F. Mun, he applied the test to 40 (males 33, females 7) formerly lepromatous patients, all in good health and nearly all bacteriologically negative for some time. A dose, beginning with 5 grains, was given every week and doubled on each occasion until in the seventh week 320 grains were given in about a pint of water. There was some complaint of the large amount to be swallowed, a few patients had transient abdominal pain, others tightness in the throat or frontal sinus pain, but corvza, lacrimation, skin eruptions, and albuminuria were absent. These results were so satisfactory that for the future it will be employed in all patients before discharge from hospital.

Moiser, B. (1940) *Leprosy Rev.* **11**, 99

Treatment

Diphtheria Antitoxin and Toxoid

D. R. Collier and J. H. McKean give a preliminary report on the treatment of approximately 110 patients who were having repeated leper reactions by (a) diphtheria antitoxin and (b) diphtheria toxoid. It was not expected that diphtheria antitoxin would cure leprosy, but that it might neutralize the leprosy toxin in the toxæmia syndrome, namely the leprosy reaction. First of all, 50 cases were injected during leper reactions with 6,000 units of diphtheria antitoxin. The immediate effect was increase in fever and general symptoms, but after 3 or 4 days improvement set in; in many cases the leprosy nodules and elevated red areas scaled over, shrank and changed from a bright red to a dark brown colour. In more acute reactions the centre of the nodule may suppurate and the leprosy bacilli become granular, suggesting polar bodies, and become quite abnormal. As controls other lepers were injected with either tetanus antitoxin or antivenom but without any effect. Later, when the improvement after the initial injection was established, repeated doses every 10 days of 2,000 units of diphtheria antitoxin were given to lepers who were not having leper reactions. When the effect of diphtheria antitoxin was shown to be beneficial cases with various types of leprosy were injected intramuscularly with diphtheria formol-toxoid in doses of 0.5 c.c.m. rising by 0.5 to 2 c.c.m. every fortnight. The following beneficial results are tabulated: immediate reduction of leper plaques, nodules, and tuberculoids, rapid improvement in leper reactions with usually lasting effects, and return of sensation in some previously anaesthetic areas; reduction of enlarged nerves, particularly the ulnars, general physical improvement, absence of any untoward effects. In an editorial addition

it is stated that out of 170 cases treated with toxoid (122 being lepromatous) 35 became negative, 70 had fewer leprosy bacilli, and 128 improved skin lesions. These results would appear excellent if it were not that in 147 controls treated with chaulmoogra alone (58 of which were of the lepromatous type) 46 became negative, 25 had fewer bacilli, and 16 improved skin lesions. Unfortunately, the subtype (L1, 2 or 3) of the lepromatous cases is not mentioned.

Collier, D. R., and McKean, J. H. (1940) *Leprosy Rev.* **11**, 140

LEUCORRHOEA AND OTHER NON-HAEMORRHAGIC VAGINAL DISCHARGES

See also B.F.M.P., Vol. VII, p. 710; Cumulative Supplement, Key Nos. 937-939, Surveys and Abstracts 1939, p. 403, and pp. 19 and 22 of this volume

Trichomonas Vaginalis

Treatment

Floraquin K. J. Karnaky advocated the following treatment in *Trichomonas vaginalis* and all vaginal infections. The vulva, vagina, and perineum are gently washed with vinegar water (5 tablespoonfuls in 2 quarts of water) and dried. One to 2 drachms of floraquin (glucose-lactose, pH 2.9) powder are then blown into the vagina, or 4 to 8 floraquin tablets are inserted, encircling the cervix, with a small plug of cotton-wool in the vulva. Thereafter the patient inserts 1 floraquin tablet, night and morning, for 12 days. No douching should be carried out during this period. After 12 days, vinegar water douches are taken twice a day between and during the next 3 menstrual periods, up to the fourth period. If a fresh vaginal smear is found to be free from *Trichomonas vaginalis*, the patient is pronounced as cured; if the smear is positive, treatment is resumed. In a series of 400 cases, 94 per cent were cured by this method.

Karnaky, K. J. (1940) *Amer. J. Surg.* **48**, 216.

LEUKAEMIA

See also B.E.M.P., Vol. VIII, p. 1, Cumulative Supplement, Key Nos. 940-955, Surveys and Abstracts 1939, p. 404; and p. 32 of this volume

Myelocytic Leukaemia

Actiology

Associated with miliary tuberculosis. H. Ulrich and H. Parks report a case of a woman aged 45 in whom there was present both myeloid leukaemia and miliary tuberculosis. She was admitted to hospital with an enlarged spleen and a leucocyte count of 180,000, with 58 per cent of myelocytes. Later, fever developed, the legs became oedematous, and a maculo-papular skin eruption appeared. In spite of treatment the condition deteriorated, and a few scattered moist râles were heard throughout the chest, with diminution of breath sounds and dullness at the right base. At necropsy the omentum, and the visceral and parietal portions of the peritoneum, were profusely studded with small, slightly elevated, greyish-white miliary lesions. Microscopical examination showed acute miliary tubercles in some parts of the lungs, and acid-fast bacilli were demonstrated.

Ulrich, H., and Parks, H. (1940) *New Engl. J. Med.*, **222**, 711.

Aleukaemic Leukaemia

M. Hynes reviews the condition variously known as aleukaemic leucopenia, or leukaemia without gross leucocytosis, on the basis of cases examined at the Middlesex Hospital during 3 years and of published work on the subject. Diagnosis depends on the results of bone-marrow puncture which are the same in leukaemia whether the blood shows leukaemia or leucopenia; thus aplastic anaemia and myelosclerosis can be excluded. The following forms are described. (i) Aleukaemic acute leukaemia, myeloid and lymphatic. Out of 23 cases of acute leukaemia at the Middlesex Hospital 7 had a normal or subnormal leucocyte count throughout

their course. (ii) Aleukaemic chronic myeloid leukaemia is frequent, formerly called leukanaemia, and in 1914 aleukaemic myelosis to distinguish it from leukaemic myelosis, the ordinary chronic myeloid leukaemia, by Hirschfeld; its diagnosis from myelosclerosis is very difficult, and even marrow puncture is not always decisive. (iii) Aleukaemic chronic lymphatic leukaemia has rarely been reported; out of 16 cases personally examined during 3 years there was leucopenia throughout their course in 4. The differential diagnosis from lymphosarcoma, in which the leucocytes and bone marrow are normal, is complicated by the terminal occurrence of acute lymphatic leukaemia after radiological treatment of lymphosarcoma, of which Kato and Brunschwig collected 17 examples.

Associated with Angina

J B I. Tombleson reports a case of aleukaemic leukaemia in a girl aged 16 years. The case had to be differentiated from Vincent's angina. The organisms were discovered in the throat, but the patient's general condition was too poor to make this disease likely. Agranulocytosis was a possible diagnosis as the patient had sore throat and extreme leucopenia. But the presence of severe anaemia, deficient platelets, and absence of any exciting cause discounted this diagnosis. The condition resembled diphtheria in that there were pallor, cervical adenitis, nasal excoriation, and a membranous condition of the nasopharynx. The case also had much in common with aplastic anaemia, but the leucopenia with agranulocytosis and large immature leucocytes served to differentiate it. Two points of interest in this case were extreme leucopenia—there were only 250 white cells per c mm. on the first examination—and the fact that the ratio between neutrophils and lymphocytes returned to normal after blood transfusion. If this ratio is ever raised, it is said to remain so. The patient improved for a time under treatment, but finally died after 5 months' illness.

Hirschfeld, H. (1914) *Z. klin. Med.*, **80**, 126.

Hynes, M. (1940) *Quart. J. Med.*, N.S. **9**, 177.

Kato, K., and Brunschwig, A. (1933) *Arch. intern. Med.*, **51**, 77.

Tomblinson, J. B. I. (1939) *Lancet*, **2**, 977.

Lymphocytic Leukaemia

Diagnosis

Sternal puncture—M. C. G. Isaacs stated that typical blood counts in lymphocytic leukaemia may be absent, and then sternal puncture may be the only means of revealing the true nature of the condition. The disease may be mistaken for such conditions as Hodgkin's disease or splenic anaemia. He reported 5 such cases. Lymphocytosis in the marrow is rare in other conditions and in 100 cases the author found it in 2 other conditions only, namely in glandular fever and in aplastic anaemias. He divided these atypical lymphocytic leukaemias into acute and chronic groups. Those in the acute group were rapidly fatal and radiotherapy did not benefit them.

Isaacs, M. C. G. (1939) *Brit. med. J.*, **2**, 1132.

Atypical Manifestations

M. M. Wintrobe and D. M. Mitchell described some atypical manifestations which may occur in leukaemia. The disease may present varying symptoms which may cause some other disease to be diagnosed. They described 15 such cases and divided them into (i) those suggesting some acute inflammatory process, (ii) those suggesting abdominal or cardiac disease, (iii) those in which the initial symptoms were referable to the bones and joints, and (iv) those in which skin lesions were the presenting symptom. In the first group were 7 cases which were first diagnosed as miliary tuberculosis, acute thyroiditis, Hodgkin's disease and other acute inflammatory conditions. In group (ii) there were 3 cases diagnosed as paroxysmal tachycardia with 'heart disease', sarcoma of the ovary, and the other case was variously diagnosed as gall-bladder disease, coronary disease, blood dyscrasia, and lymphoblastoma. In the third group there were also 3 cases, the first diagnosed as myeloid leukaemia and presenting pain and rigidity in the back. The other 2 cases both had pains in the bones and joints and were diagnosed as chloroma

and subleukaemic leukaemia respectively. The bony pain in these cases is due to leukaemic infiltration under the periosteum. In the fourth group there were 2 cases. The first presented erythema of the skin and subcuticular masses. It was diagnosed as leukaemia. The second case had lumps in the breasts, and was thought at first to be a case of malignant disease with metastases in the bone marrow. All 15 cases were ultimately diagnosed as leukaemia on autopsy or by blood examination. Wintrobe and Mitchell also considered other cases in the literature, which from their presenting symptoms and signs could be considered as those simulating diseases of the nervous system, those simulating diseases of the chest, and those simulating diseases of the genito-urinary system.

Wintrobe, M. M., and Mitchell, D. M. (1940) *Quant. J. Med.*, **9**, 67.

Iron Content of Serum

R. Stodtmeister and P. Buchmann studied the iron content of the serum in 4 cases of chronic myeloid leukaemia and in 1 of lymphatic leukaemia. They found that, with progressive deterioration of the general condition, the iron content decreases, but that it does not keep parallel with the haemoglobin content and the leucocyte count. If, as a result of X-irradiation, the general condition improves, the iron content also noticeably increases. If the iron content remains low, the patient's condition generally shows no improvement. Deficiency of iron ultimately affects erythropoiesis, and a secondary anaemia results. The authors concluded that the iron content of the serum was a reliable indicator of the general condition, but, in view of the considerable fluctuations in the former which occur, a series of estimations is necessary.

Stodtmeister, R., and Buchmann, P. (1939) *Klin. Wschr.*, **18**, 1365.

Leukaemia in Children

Radiological Changes in the Bones

C. G. Teall, working at the Birmingham Children's Hospital and associated with I. G. Parsons, gives an illustrated account of the radiological appearances in children with leukaemia, which is said to be nearly always aleukaemic. The changes may be difficult to distinguish from those of haemolytic anaemia (see p. 171). The earliest radiological sign is a streaky type of absorption in the long bones, which may not be very striking and occasionally is seen in children without leukaemia. The long bones may show a pathognomonic generalized osteoporosis, which may also occur in the spine. Leukaemic metaplasia may separate the periosteum from the shaft.

Teall, C. G. (1939) *Brit. J. Radiol.*, **12**, 607.

Treatment

Uraemia following X-ray Therapy

D. Merrill reported 3 cases of uraemia following X-ray therapy of leukaemia, and maintained that this was not a rare complication. It had been shown that X-ray treatment of myeloid or lymphatic leukaemia resulted in an enormous increase of uric acid in the body which had to be excreted by the kidneys. This increased burden might conceivably precipitate clinical uraemia, if the kidneys were sufficiently damaged either by leukaemic infiltrations or by non-leukaemic lesions. As a means of minimizing the danger of leukaemia, the following regime was suggested, a study of the blood levels of non-protein nitrogen and uric acid and of the 24-hour urinary excretion of uric acid should be made before beginning X-ray treatment. A low-purine diet and liberal quantity of fluid should be given during X-ray treatment. Alkalis should be given by mouth in an attempt to keep the urine alkaline and thus lessen the danger of uric acid calculus formation. Cinchophen should be given before X-ray treatment in cases with a high blood uric acid, because of its effect in increasing the excretion of uric acid in cases of gout and leukaemia. Blood uric acid and 24-hourly urinary uric acid output determinations should be made every 3 or 4 days during X-ray treatment, as a guide to increasing or decreasing the frequency of treatment. X-ray treatment should be given in small doses, and it should first be applied directly to the kidneys in order to remove

leukaemic infiltration and thus increase renal function before loading the kidneys with uric acid from X-ray treatment applied in other bulky leukaemic deposits such as those in the spleen and bone marrow.

Merrill, D. (1940) *New Engl. J. Med.*, **222**, 94

LICHEN

See also B.E.M.P., Vol. VIII, p. 41; Cumulative Supplement, Key Nos. 956-960, and Surveys and Abstracts 1939, p. 405

Lichen Planus

Clinical Picture

D. W. Montgomery states that lichen planus of the palms may be a distinctly papular eruption, only slightly itchy. The papules may be arranged in circles so as to resemble completely a papular syphilide. The papules, moreover, may so closely resemble vesicles as to be regarded as eczema or cheilopompholyx. In other cases the congestion may be more intense, and the eruption may be really vesicular, or even bullous. In other cases still it may be even more intense, becoming pustular and resembling scabies. Finally, the horny surface of the palms may be thick, rugous, and patchy, resembling callosities.

Montgomery, D. W. (1940) *Urol. cutan. Rev.*, **44**, 249

LINDAU'S DISEASE

See also B.E.M.P., Vol. VIII, p. 55

Clinical Picture

Angiomatosis Retinae

X-ray therapy—F. C. Cordes and M. J. Hogan give an account of angiomatosis retinae (von Hippel's disease) and report a case treated by X-rays. The condition is an angiomatous tumour surrounded by glial tissue, and has been considered as primarily gliomatous with vascular proliferation. Von Hippel, however, showed that it is a true angiomatosis of the central nervous system such as may occur in the brain. It may be generalized, cysts forming in the cerebellum, pancreas, and kidney—Lindau's disease—with which it has been associated. The retinal site is commoner in males, mainly in young adults, and is often familial. It is bilateral in 50 per cent of cases and the prognosis is poor. In the early stages the diagnosis is easy until detachment of the retina follows. Coats's disease and angioma of the choroid must be differentiated from it. Irradiation, with X-rays and radium, has been used in treatment by other workers but is often unsuccessful. Cordes' and Hogan's patient was treated at an early age with high voltage X-rays, and after 7 months' treatment the vessels and the exudate diminished. From this, and the reported results it is concluded that it should be treated by irradiation, provided there are not any angiomatous lesions elsewhere.

Cordes, F. C., and Hogan, M. J. (1940) *Arch. Ophthalm.*, N.Y., **23**, 253

LIVER DISEASES: LIVER FUNCTION TESTS

See also B.F.M.P., Vol. VIII, p. 81, Surveys and Abstracts 1939, p. 406, and p. 166 of this volume

Galactose Tolerance Test

N. F. MacLagan finds that the galactose tolerance test of the glycogenic function of the liver is preferable to the laevulose test, both on theoretical grounds as expressed by F. C. Mann, and because in practice the estimation of blood-galactose is much easier than that of blood-laevulose. The patient is starved overnight, no breakfast or morning tea being allowed; 40 g. of galactose, dissolved in 250 c.cm. of water is given by mouth; in order to obtain complete solution hot water must be used and cooled subsequently. Blood is collected into fluoride or oxalate tubes

$\frac{1}{2}$, 1, $1\frac{1}{2}$ and 2 hours after the solution is swallowed, and estimated by a specially modified method and expressed as the 'galactose index' (G.I.). A satisfactory differential diagnosis was given in 16 cases of jaundice; all the toxic and none of the obstructive cases showed impaired hepatic function. Many poisons, e.g. of toxic goitre, affect the glycogenic function much more than the excretory ones, and many cases of hepatic cirrhosis fall into this category. The clinical value of the test depends upon its power of testing one function of the liver which is independent of the excretion of bile, thus the cases of obstructive jaundice, without any evidence of impaired galactose function, gave an average of 12.9 mg. of bilirubin per 100 c cm, whereas the cases of toxic jaundice, all with impaired galactose function, had an average serum-bilirubin of only 5.4 mg. per 100 c cm.

MacLagan, N. I. (1940) *Quart. J. Med.*, N.S. **9**, 151.

Mann, F. C. (1934) *Ann. intern. Med.*, **8**, 432.

Colloidal-Gold Reaction

S. J. Gray studied the colloidal gold reaction of the serum in 96 cases of hepatic disease, comprising 46 of cirrhosis, 14 of acute parenchymatous disease, 25 of new growth, and 11 of miscellaneous hepatic diseases. The diagnoses were confirmed by necropsy, biopsy, and laparotomy in 34 cases, 11 in the first group; 2 in the second, 13 in the third, and 8 in the fourth. The reaction was positive in all the 46 cases of cirrhosis, in 13 of the 14 cases of acute parenchymatous involvement, in 19 of the 25 cases of neoplasm, and in all 11 cases of miscellaneous hepatic disease. In some of the cases the test detected liver disease, not discovered by the usual clinical and chemical tests, and later confirmed by operation or necropsy. The test was negative with sera from 20 normal adults, and in 73 of 75 cases of various extrahepatic diseases. In 22 of these cases normal livers were found at necropsy, biopsy, or laparotomy. Positive reactions were obtained in 8 of 20 cases of syphilis; in 1 of these 8 there was a history of hepatitis, but in the others there was no apparent hepatic disease. The Takata-Ara reaction was positive in only 34 of 58 cases of hepatic disease (58.6 per cent); it was therefore considerably less sensitive than the colloidal gold reaction. The total plasma cholesterol was normal in 38 of 77 cases of hepatic disease.

Gray, S. J. (1940) *Arch. intern. Med.*, **65**, 524.

Hippuric Acid and Prothrombin Tests

A. J. Quick described a hippuric-acid test for liver function. If benzoic acid is ingested it combines with glycine and forms hippuric acid which is excreted in the urine. This chemical change is performed in the liver, and a measure of the hippuric acid excreted is a measure of the liver's efficiency. Sodium benzoate is given by mouth or intravenously and the amount of hippuric acid excreted over a fixed period is measured. Besides assessing liver function the test is of use in differential diagnosis, in establishing the prognosis and evaluating the treatment in various hepatic diseases, and in the study of the physiology of the liver. Quick also described a quantitative test for prothrombin. The clotting-time is a measure of the prothrombin, provided the other factors in the blood producing clotting are made constant. The clotting-time is measured after an excess of thromboplastin has been added to oxalated blood which is recalcified with a fixed quantity of calcium chloride. It has been found that vitamin K is necessary to the formation of prothrombin. It is not formed if the intake or absorption is inadequate. The intake makes no difference, except in the case of newly-born infants, because the vitamin is synthesized by the intestinal flora. There are no such organisms in the newly-born and vitamin K must be given by mouth, if necessary, to prevent haemorrhagic disease. In the adult, diseases of the biliary tract interfere with absorption since bile is necessary for it. Vitamin K and bile salts must be given to make good the deficiency in this condition. Diseases of the liver interfere with the synthesis of prothrombin. Unless the liver function is improved such cases respond poorly to treatment with vitamin K and bile salts.

Quick, A. J. (1940) *Amer. J. clin. Path.*, **10**, 222.

The Serum Choline Esterase

B. McArdle investigated the serum choline esterase in jaundice and diseases of the liver. In 40 normal adults the choline esterase in the blood serum ranged from 51 to 121 units (Tod and Jones), the average being 78 units. In children the average was 105 units. In 71 cases of liver disease the average value was only 36 units. In 21 of 24 cases of obstructive jaundice the value was 50 units or above. If the jaundice was due to liver disease the value was below 50 units in 33 of 38 cases. McArdle suggested that the choline esterase index might be used as another means of differentiating obstructive and hepatic jaundice. When the liver function recovered the index rose with it. A variety of other diseases produced varying values, but in those in whom some liver damage was suspected the index was always below 50 units. The test, therefore, can also be used in the diagnosis of liver disease.

McArdle, B. (1940) *Quart. J. Med.*, **9**, 107.

LIVER DISEASES: HEPATITIS, CHRONIC

See also B E M P., Vol. VIII, p. 118, Cumulative Supplement Key No. 974, Surveys and Abstracts 1939, p. 409; and p. 28 of this volume.

Aetiology

W. C. Von Gilahn and I. B. Flinn investigated the effect of adding powdered brewers' yeast to the diet of rabbits receiving lead arsenate. The lead arsenate was given to induce experimental cirrhosis of the liver. Four controls were given a standard diet, 5 rabbits were given a standard diet plus yeast, 5 rabbits a standard diet plus lead arsenate, and 13 rabbits a standard diet plus yeast and the arsenate. Another series of 7 rabbits were given the diet and larger doses of the arsenate. It was found that brewers' yeast reduced the incidence of liver cirrhosis produced by the arsenate. Only 46 per cent developed cirrhosis when they were receiving yeast, whereas in the group receiving only the arsenate the incidence was about 85 per cent. The amount of glycogen in the liver bore no relation to the incidence of cirrhosis or to the amount of arsenic found in the liver.

Deficient Diet

A. R. Rich and J. D. Hamilton produced experimentally in rabbits a cirrhosis of the liver resembling Laennec's cirrhosis. A group of 14 rabbits fed for 25 to 113 days on a diet supplemented by various vitamins, but lacking yeast, developed the cirrhosis, in seven there was ascites, and in two gall-stones. The amount of protein, fat or carbohydrate in the diet did not affect the result. No other vitamin-lack was found to be implicated in the causation of the condition. If vitamin B₁, B₂, B₆, or nicotinic acid were added to the diet the cirrhosis still developed; it must therefore be some other factor in the yeast, so far unknown, but possibly choline.

Rich, A. R., and Hamilton, J. D. (1940) *Johns Hopk. Hosp. Bull.*, **66**, 185.
Von Gilahn, W. C., and Flinn, I. B. (1939) *Amer. J. Path.*, **15**, 771.

Hepatic Cirrhosis in Children

R. Priesel and I. Schuler reported 22 cases of hepatic cirrhosis in early childhood, 11 being observed by themselves. In no case was the child over 2 years of age. The onset of the disease was generally insidious, with anorexia, drowsiness, and fretfulness. There occurred emaciation and abdominal distension, due partly to enlargement of liver and spleen. In the later stages there was generally jaundice. Most of the cases had a raised temperature. There were severe anaemia, and leucocytosis up to 56,000. The prognosis was poor, most of the children dying within a few months. With regard to aetiology syphilis was present in two. Alcoholism in the parents and tuberculosis played no part. Neither typhoid nor paratyphoid fever could be discovered either clinically or by laboratory methods. In the authors' opinion hepatic cirrhosis in young children was due to infection.

by an unknown organism. In several cases there appeared to be a familial disposition, one person having lost 4, and his brother 3, children from the disease.

Priesel, R., and Schuler, F. (1939) *Wien. klin. Wschr.*, **52**, 840.

LIVER DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 151.

Benign Tumours

Congenital Cyst of the Round Ligament of the Liver

R. Lightwood and L. I. Campbell report the case of a male child, weighing 8½ lb at birth, who soon after birth became cyanosed with an enlarged abdomen. As ascites seemed probable, the abdomen was tapped and 320 c.cm. of straw-coloured fluid were removed. When 8 weeks old, the infant weighed 10 lb. 6 oz., and was found to be oedematous in the lower limbs and the scrotum, especially on the right side, an elongated elastic tumour thought to be a hydronephrosis until an intravenous pyelogram showed that the renal calyces were normal, was palpable on the right side of the abdomen. The urine contained a trace of albumin and many renal epithelial cells. Death was due to an intercurrent infection ending in gastro-enteritis. At necropsy there was a large sausage-shaped cyst, evidently in the round ligament of the liver, containing alkaline fluid. There was not any evidence of a teratoma. Two other recorded examples of this very rare condition were quoted, in a man aged 41 (Henderson) and a woman aged 54 (Wakeley and Macmyn).

Lightwood, R., and Campbell, L. I. (1939) *Lancet*, **2**, 1027

Henderson, M. S. (1909) *Ann. Surg.*, **1**, 550

Wakeley, C. P. G., and Macmyn, D. J. (1931) *Lancet*, **2**, 675

LUNG DISEASES: ATELECTASIS AND COLLAPSE

See also B.F.M.P., Vol. VIII, p. 160, and Cumulative Supplement, Key No. 985

Aetiology

Allergy

T. B. Friedman and C. J. Molony investigated the role of allergy in atelectasis in children. They reported 6 cases of non-postoperative, non-traumatic atelectasis and one case of post-operative atelectasis occurring in allergic children. The authors stated that the atelectasis could be produced by bronchial obstruction in allergic subjects. The bronchial obstruction might be due to: (i) spasm of the bronchial musculature, (ii) thickening of the walls of the bronchi and bronchioles from oedema, hyperplasia, hypertrophy, and cellular infiltration, (iii) secretion of very thick tenacious mucus, and (iv) paradoxical collapse of the bronchi during expiration. The authors considered treatment of the condition under two headings. During the attack adrenaline should be given to relax the bronchi. Mucus should be removed with expectorants and, if these fail, by bronchoscopic aspiration. To prevent further asthmatic seizures a thorough allergic study must be done to determine the cause, and suitable treatment then instituted. It is thought by some that these attacks of atelectasis may subsequently produce bronchiectasis.

Friedman, T. B., and Molony, C. J. (1939) *Amer. J. Dis. Child.*, **58**, 237

Post-Operative Atelectasis

Treatment

Bronchoscopy.—J. A. Perrone stated that the predominating post-operative pulmonary complication is atelectasis. Early recognition is important because it allows an earlier institution of treatment and facilitates a more prompt return to normal of the atelectatic lobe, and it obviates post-operative pneumonia which may occur in atelectasis of longer duration. The most important factor in producing atelectasis is bronchial obstruction, and its removal can be achieved most satis-

factorily by bronchoscopic aspiration. Once the obstruction is removed, the lung reinflates. Following bronchoscopic aspiration, patients receive almost instantaneous relief, with a marked drop in temperature, and in pulse and respiratory rates.

L. H. Mousel discussed the bronchoscopic treatment of post-operative atelectasis. He considered that most cases of post-operative broncho-pneumonia are actually cases of atelectasis. He thought, too, that most cases are due to bronchial plugging with tenacious mucus or inhaled blood during anaesthesia. In massive atelectasis there is mediastinal displacement; in the milder cases, discomfort on the affected side, tachycardia, pyrexia, and cyanosis occur. For successful bronchoscopic aspiration, the condition must be recognized and treated early, before stagnation leads to broncho-pneumonia. If changes of posture and inhalation of 5 to 10 per cent carbon dioxide fail to relieve atelectasis rapidly, bronchoscopic drainage is immediately indicated. The author described 3 cases successfully treated, in each of which the atelectasis was shown first radiologically.

Mousel, L. H. (1940) *Proc. Mayo Clin.*, **15**, 261

Perrone, J. A. (1940) *Ann. Otol., etc., St. Louis*, **49**, 528

LUNG DISEASES: ABSCESS AND GANGRENE

See also B.E.M.P., Vol. VIII, p. 172; Cumulative Supplement, Key No. 987, and Surveys and Abstracts 1939, p. 410.

Aetiology

A. M. Fisher and G. G. Finney analysed 88 cases of lung abscess, of which 57 per cent were, at the time of the report, well or improved, and 41 per cent dead. In the majority of cases atelectasis and aspiration appeared to be of fundamental importance in the pathogenesis. Embolism accounted for a much smaller number. The majority of cases in this series were due to respiratory infections (49 per cent), while 26 per cent were post-operative. It was found that the bacteria in the abscesses were predominantly anaerobic, with anaerobic streptococci and Gram-negative bacilli predominating. Surgical treatment should be considered when a patient fails to show improvement after approximately 3 to 5 weeks of conservative treatment.

Fisher, A. M., and Finney, G. G. (1940) *Johns Hopk. Hosp. Bull.*, **46**, 263

LUNG DISEASES: TUBERCULOSIS

See also B.E.M.P., Vol. VIII, p. 182; Cumulative Supplement, Key No. 988, Surveys and Abstracts 1939, pp. 114 and 411; and p. 94 of this volume.

Diagnosis

Stomach Lavage

From the investigation of 1,000 patients, A. Stadnichenko *et al.* assess the value of gastric lavage in the control and treatment of tuberculosis. The stomach was aspirated in the morning through an Lwald tube after the patient had drunk 4 ounces of sterile distilled water, no food or other drink being allowed before the aspiration. The aspirated fluid was then centrifugalized, examined, and injected into guinea-pigs. Gastric lavage is a very reliable method for the detection of tubercle bacilli. Negative results are always obtained in those with healed lesions and in those with some other disease. Results are also negative in very early lesions and in those with closed lesions in the lungs, in which bacilli do not enter the larger bronchi. In the control of collapse therapy, especially when the lung is re-expanding, gastric lavage is very useful, and should be repeated at frequent intervals as one negative result is not conclusive. It was concluded that even if the sputum is negative, the patient with tuberculosis should not be considered cured until gastric lavage has also been negative.

Stadnichenko, A., Cohen, S. J., and Sweany, H. C. (1940) *J. Amer. med. Ass.*, **114**, 634.

Differential Diagnosis

Tuberculosis of Nasopharynx

J. W. Trenis, recognizing that tubercle bacilli may enter the sputum from lesions of the tracheo-bronchial tree, as apart from the lung parenchyma, reports 2 cases suggesting that still another source of tubercle bacilli in the sputum should receive more serious clinical study. In both of these patients there were tuberculous lesions of the nasopharynx, both expectorated the sputum in the characteristic manner for post-nasal discharge, in both the sputum contained readily demonstrable tubercle bacilli; and in one, frequent X-ray examinations of the chest, and a bronchoscopic examination, were negative for evidence of tuberculosis. The author concludes that, when X-ray examination of the chest fails to show evidence of tuberculosis, or when the chest changes present do not serve as a satisfactory explanation of tubercle bacilli in the sputum or gastric contents, a tuberculous lesion in the posterior nasopharynx as well as one in the tracheo-bronchial tree should be suspected as the site of origin of the bacilli.

Trenis, J. W. (1940) *Amer. J. med. Sci.* **43**, 312.

Treatment

Ascorbic Acid

Many workers have found a state of vitamin-C unsaturation in pulmonary tuberculosis. G. S. Erwin *et al.* investigated this problem in 24 acute or bronchopneumonic cases, and in advanced chronic cases. They also assessed the value of ascorbic acid in the treatment of pulmonary tuberculosis. They found that urine analysis showed the daily excretion of ascorbic acid to be below normal in all cases. Full saturation with vitamin C had no effect upon the progress or complications of the illness. Eleven of the patients died during the investigation and several patients had haemoptyses, one of which was fatal. The authors concluded that the vitamin-C unsaturation is not specific in pulmonary tuberculosis, but is the same as is found in many other states of toxæmia.

Sulphanilamide

L. B. Freilich *et al.* investigated the action of sulphanilamide in chronic pulmonary tuberculosis. Thirty-five patients were treated for a period of 10 to 15 weeks, the initial dose of the drug being 10 g., three times a day, with equal amounts of sodium bicarbonate; this dosage was increased until, by the end of a month, 20 g. were being given. No other therapeutic measures were employed. No improvement occurred in any case, neither was any influence exerted on extra-pulmonary complications. Toxic effects, particularly headaches, were numerous. The authors consider that the results are not very surprising seeing that the chief success of sulphanilamide is in acute blood-borne or lymph-borne conditions, and that in tuberculosis the lesions are relatively avascular and protected by fibroblasts and epithelioid cells.

Sulphapyridine

S. T. Allison and R. Myers record 7 cases of active pulmonary tuberculosis and one case of generalized miliary tuberculosis treated with sulphapyridine. The total dosage varied from 108 g. to 5 g. In 4 cases it was necessary to withdraw the drug because of toxic symptoms. Nausea occurred in 5 of the cases, vomiting in 3, and haematuria in one. The haematuria was due to the formation of a calculus which lodged in the upper portion of the left ureter. Two patients died, and in one the disease spread rapidly after the patient had received 103 g. of the drug. It thus appeared that sulphapyridine did not influence the course of the disease.

Artificial Pneumothorax

Accidents and complications—P. M. Mattill and F. L. Jennings made a study of the complications which occurred in 1,171 patients who, between 1917 and 1936, were submitted to artificial pneumothorax. The authors are rather sceptical of the condition known as 'pleural shock' which they think may be due to a pulmonary embolus. Air embolism they found to be excessively rare, occurring only twice in the course of over 50,000 pleural punctures. Accidental pneumothorax was seen

in 3 per cent of patients in the unilateral group, and in 21 per cent of the bilateral. In the bilateral cases there were 5 resulting deaths. In unilateral cases, however, it was not a serious condition. Mediastinal hernia was a complication in 9 per cent of the series, the protrusion always being directed anteriorly.

A study was made of selected patients to determine the time of formation of pleural fluid. In 26 per cent of cases it was formed within the first month of treatment, and in 77 per cent within the first 6 months. Of the clear effusions 72 per cent, as tested by guinea-pig inoculation, contained tubercle bacilli. Empyema formed in 14.3 per cent of all pneumothorax patients and in 27 per cent of all effusions of the 131 patients so affected, 71 are dead, 48 having died within 3 years of the commencement of pneumothorax treatment. Mortality was particularly high in those who developed a bronchopleural fistula. Pulmonary re-expansion with the induction of collapse by thoracoplasty, by phrenic avulsion, or even by surgical obliteration of the empyema cavity, gave the best therapeutic results.

Rate of conversion of sputum—R. A. Bendove *et al.* demonstrate that the greatest number of conversions from positive to negative sputum following the provision of artificial pneumothorax therapy occurs in the early months of treatment. More than 90 per cent become negative within the first six months, and there are few converted cases after the ninth. Left-sided cases yield a slightly higher percentage conversion (10 per cent).

If the duration of tuberculosis prior to pneumothorax induction is 6 months or less, there is an 80 per cent chance of conversion from positive to negative within 3 months. The younger the patient the better is the outlook. Low intrapleural pressures are just as effective as high in suppressing tubercle bacilli in the sputum.

Differential diagnosis of acute abdominal conditions—R. H. Bennett and B. Burbank emphasized the difficulty of deciding, during pneumothorax therapy, whether an apparent abdominal pain is really of abdominal or of thoracic origin. Three special points are of assistance in distinguishing the onset of an acute pleurisy from an acute appendix: (i) reference of pain to the areas innervated by the seventh to the twelfth dorsal nerves, thus affecting the lower part of the chest and lumbar region in addition to the abdomen, (ii) in pleurisy the respiration rate is increased out of all proportion to the pyrexia, and (iii) the initial abdominal symptoms of pleurisy, particularly vomiting, are apt to be more severe than those seen with the average acute appendix.

Treatment of complications—F. Dumarest and P. Pavie discuss the value of pleurotomy in the treatment of complications of artificial pneumothorax. The 3 risks involved in incision of the tuberculous pleura are: secondary infection of the serous membrane, deterioration of the body as a whole from prolonged suppuration, and the poor power of repair in healing of a thoracic fistula. There is, however, practically very little danger of secondary infection of the pleura which has a very high resistance, and the bacteria that might enter from the skin are of very low pathogenicity. With regard to prolonged suppuration, this decreases in time considerably. For example, in one case after 5 years of drainage, one daily drainage amyloidosis never occurred. The third objection, i.e. permanence of the secondary infection. Clinical experience shows that drainage, instead of reducing the patient to a cachectic state, increases the weight. In their cases of continuous drainage amyloidosis never occurred. The third objection, i.e. permanence of the pleural fistula, is also not supported by clinical evidence, spontaneous closure of the fistula was noted in 20 per cent of their cases, and this incidence may be raised by surgical treatment. Pleurotomy constitutes the only means of protecting the non-infected (or less infected) part of the lungs from infection or re-infection in a case of a perforated pneumothorax. Owing to some unexplained mechanism, there is also a definite curative effect upon the lesions in the other parts of the lungs. This surprising fact is proved by some case histories. Pleuro-pulmonary fistulae sometimes close, but often large ones remain open without causing any inconvenience or having any influence upon the patient's general state. The malignant type of purely tuberculous pleurisy should always be treated with pleurotomy.

In psychotic patients—E. F. Dombrowski *et al.* discuss the part played by artificial pneumothorax in the treatment of pulmonary tuberculosis in psychotic patients. Of 68 such patients, 40 underwent artificial pneumothorax, 10 were in an arrested state, and the remainder were, at the time of the report, under consideration for

other forms of treatment. Previous reports had shown that patients with functional psychoses and tuberculosis were usually treated by rest and that nothing else was directed to prevent the progress of the tuberculous disease. All the 40 patients greatly improved; a very good result was obtained in those with a toxic psychosis induced by tuberculosis. The treatment was combined with narcosis after the temperature became normal. This also had a good effect on the mental state. A good general diet containing vitamin D and calcium was also given. Five of the patients are reported in detail. The pneumothorax has a good effect upon the emotional and psychic outlook and shortens the period of hospitalization.

End-results.—F. Tice and A. J. Hruby surveyed the results of collapse therapy in 8,083 cases of tuberculosis. Of 7,341 patients, 3,090 were treated with collapse of the lung for more than 3 months, 337 for less than 3 months, 330 had artificial pneumothorax attempted, and 3,584 were controls; 742 patients were not considered as their records were incomplete. The results in the treated group were found to be about twice as good as the controls. Compared with the usual expectation of life in those suffering from open tuberculosis, the results were very good, the results were rather better in those who had undergone combined collapse (two or more procedures) than in those who had only been subjected to one operation. The survival-rate was rather better in those treated in a clinic. The results were best of all when the two treatments were combined. In the Negro the results were not so good as in the white races, possibly because the facilities for in-patient treatment are not so good for Negroes. Tice and Hruby concluded that collapse of the lung is a very good method of treating open pulmonary tuberculosis, especially as it can be successfully used as an out-patient measure.

Partial Collapse Operations

A. L. D'Abreu discusses the operations for partial collapse in pulmonary tuberculosis. Of the major surgical procedures he considers total thoracoplasty (1 to 10 ribs) to be the most efficient. In 16 patients so treated, all with cavities, there were no deaths and 15 of them became sputum-free or retained only a trace of negative sputum. The results were not so good in 'partial thoracoplasty' and extrapleural pneumothorax, the superiority of total thoracoplasty being ascribed to the patient's condition. Most patients submitted to the operation are in a chronic state and therefore with a good resistance to the disease, and the cavities are usually accompanied by a good deal of fibrosis. The chief risks in partial thoracoplasty are that the collapse of the lung may be insufficient and the disease may spread to the lower lobe. These risks may be lessened by early operation and by operation under a local anaesthetic. The local anaesthetic prevents the loss of the cough reflex for any time and therefore reduces the chance of bronchogenic spread and of atelectasis. D'Abreu considered that an uncollapsed cavity, even though the patient appears well, usually proves fatal. If all other methods fail to collapse it, the patient should be submitted to thoracoplasty. Phrenic nerve operations are most useful in soft-walled cavities, and as preliminaries to more extensive surgical procedures which are not advisable at the time, owing to some adverse factor such as repeated haemoptysis. D'Abreu did not advise apicolysis with plombage or very limited thoracoplasties because they do not close chronic cavities. Partial thoracoplasty should be done in all cases of large chronic cavities, surrounded by at least 2 cm. of fibrosis, and producing a positive sputum. The general condition of the patient should be good. A pyo-pneumothorax below the chronic cavity in the upper lobe is also an indication for this operation. Contra-indications include failure to respond to rest in bed, the presence of active disease elsewhere in the lung, and the complication of a general disease, such as nephritis. Extra-pleural artificial pneumothorax is indicated for soft-walled apical cavities, which do not respond successfully to artificial pneumothorax, and for patients who are unfit for thoracoplasty, either by reason of their age or because of active disease in the other lung. Extra-pleural artificial pneumothorax in conjunction with intra-pleural artificial pneumothorax is not usually a good treatment for pulmonary tuberculosis with vomicae on account of the danger of infection and haemorrhage.

Paraffin-Pack Apicolysis

F. Ottaviano employed extrapleural apicolysis by means of the paraffin pack in 25 cases of pulmonary tuberculosis. The paraffin employed, which had a melting

point of 47° to 58° C., was treated with vioform (iodochlorhydroxyquinoline) in the proportion of 200 parts of paraffin to 1 part of vioform. The technique was simple. Under local anaesthesia a small incision, 3 to 4 inches long, was made posteriorly through the soft tissues down to the ribs. About 1½ to 2 inches of the third or fourth rib was resected. The pleura was stripped away carefully with the finger. The paraffin, which had been allowed to cool to a point at which it was just malleable, was made into small sausage-shaped masses and inserted gently without undue pressure. The soft tissues were then carefully united to prevent bulging of the paraffin. In the more or less ideal type of case (apical unilateral or bilateral active lesions with inactive not very extensive tuberculosis in the opposite lung), of which there were 4, all had negative sputum after the operation. One died, but the paraffin packing was apparently not responsible. In the favourable group (minimal or moderately advanced unilateral lesions, extending below the limits of the apex, or present in other regions, one-stage thoracoplasties and cases with negative sputum, but with frequent haemoptyses), of which there were 8, only one case did not become negative. In the questionable group (poor thoracoplasty risks and two-stage thoracoplasties whose sputum had not turned negative, advanced tuberculosis, etc.), of which there were 14, 6 had negative sputum and 7 maintained positive sputum. The author considered that this method had a place in the treatment of tuberculosis.

Internal Pneumolysis

F. I. Wollaston reports the results obtained in 200 cases of pulmonary tuberculosis treated by internal pneumolysis. The object of the treatment is so to divide adhesions as to obtain satisfactory collapse of the lung in artificial pneumothorax. It has been shown that efficient collapse, which is essential to treatment, only occurs without division of adhesions in those cases with very slight disease. Adhesions may also cause trouble after the artificial pneumothorax has been stopped. In most of the cases in this series there was a large uncollapsed cavity with positive sputum. After treatment 86 per cent of them were well and with a free lung down to the aortic knuckle, and in only 20 cases was the sputum positive. Thoracoscopy was undertaken and adhesions were divided in these patients 6 to 8 weeks after induction of artificial pneumothorax. X-ray examination was very unreliable in establishing the character of an adhesion. Adhesions may be roughly divided into 3 groups: (i) Fibrous bands and veils containing no visible lung; (ii) thick bands which may contain visible lung, and (iii) large areas of directly adherent lung. In the first group adhesions can be easily and safely divided. The divisibility in the second group depends upon how far the lung extends towards the chest, and on the anatomical site of insertion of the band (whether near the great vessels in the mediastinum). Adhesions in the third group are usually indivisible. Shock and pain are very small in this operation and empyema and pleural effusion are no commoner than in other pneumothorax cases. Haemorrhage, which is the most alarming complication, usually comes from the chest wall and as a rule can be controlled by diathermy even if coming from a large vessel. Wollaston concludes that thoracoscopy should be done on every partial pneumothorax, and it should be possible to divide adhesions, if necessary, in every sanatorium.

Temporary Elimination of Some Intercostal Nerves

J. Torek reports on the treatment of pulmonary tuberculosis by the temporary elimination of several intercostal nerves. The object of the treatment was to provide functional rest to the affected part. The skin of the intercostal space was first injected with novocain and then 2 c.cm. of alcohol injected into the nerve. The injections were usually made below the 3rd, 4th, 5th, and 6th ribs on both sides. The nerves did not undergo regeneration until about 2 months after the injection. The procedure was repeated at 3 to 4 monthly intervals for at least 2 years and was not discontinued until clinical cure was apparent. The general condition usually improved in about 3 months, and was followed by diminution of cough expectoration, and finally by disappearance of tubercle bacilli from the sputum. In one fibrosclerotic case the improvement was immediate. The treatment had an immediate good effect upon haemoptysis. Torek considers that the treatment has practically unlimited indications. It is very useful in cases in which it is impossible to establish a pneumothorax owing to adhesions, and in haemoptysis.

It is also strongly indicated in early cases, when it is doubtful whether a pneumothorax is necessary, and in severe late cases when the general condition is too poor to stand any other operative procedure

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 Bendove, R. A., Alexander, H., Deren, M. D., and Lipstein, S. (1940)
Amer Rev Tuberc, **41**, 177.
 Bennett, R. H., and Burbank, B. (1940) *Amer Rev Tuberc*, **41**, 50.
 D'Abreu, A. L. (1940) *Brit J Tuberc*, **34**, 27.
 Dombrowski, E. F., Rankin, F. S., and Goldstein, H. H. (1940)
J nerv ment Dis, **91**, 449.
 Dumarest, F., and Pavie, P. (1939) *Pr. méd.*, **47**, 1285.
 Irwin, G. S., Wright, R., and Doherty, C. J. (1940) *Brit med J*,
1, 688.
 Freilich, I. B., Coe, G. C., and Wien, N. A. (1939) *Ann intern Med*,
13, 1042.
 Mattill, P. M., and Jennings, I. I. (1940) *Amer Rev Tuberc*, **41**, 38.
 Ottaviano, I. (1940) *Amer Rev Tuberc*, **41**, 334.
 Tice, F., and Hruby, A. J. (1939) *J Amer med Ass*, **113**, 101.
 Torek, J. (1939) *J. thorac. Surg*, **8**, 607.
 Wollaston, F. L. (1940) *Brit J Tuberc*, **34**, 13.

LUNG DISEASES. TUMOURS

See also B. I. M. P. Vol. VIII, p. 224, Cumulative Supplement, key Nos. 992-994, and Surveys and Abstracts 1939, pp. 115 and 415.

Non-Malignant Intrathoracic Tumours

Cyst of Pleura

W. Addey reports a case in a woman, aged 49, with dyspnoea and palpitation for some years and becoming worse lately. X-ray examination showed a small oval pulsatile mass in contact with the heart in the right cardiophrenic angle, which probably communicated from the heart. It was thought to be a tumour of the middle lobe of the right lung, a pericardial cyst, or a chondroma. Operation enabled a simple cyst projecting from the anterior layer of the pleura to be successfully removed. Of this very rare condition 16 examples are stated to have been recorded.

Addey, W. (1940) *Brit J Radiol*, N.S., **13**, 180.

Malignant Tumours of Lungs and Bronchi

Cutaneous Metastasis in Bronchogenic Carcinoma

H. Charache reports a case of primary carcinoma of the left bronchus with an unusually large secondary growth—the size of a grapefruit—on the same side of the chest. Cutaneous metastases in bronchogenic carcinoma have been seldom recorded, among 1,063 cases previously reported of bronchogenic carcinoma cutaneous metastases were mentioned in 30, or 3 per cent, only, in a majority of which they were on the same side of the body as the affected bronchus. Not only are they usually small, but they may appear at a considerable distance from the chest, and so may escape notice. A biopsy of these metastases may in obscure cases be of diagnostic value.

Charache, H. (1939) *Amer J Cancer*, **37**, 431.

LUNG DISEASES: POST-OPERATIVE COMPLICATIONS

See also B. I. M. P., Vol. VIII, p. 235; Surveys and Abstracts 1939, p. 417; and p. 108 of this volume.

Pulmonary Embolism

Diagnosis

A. S. Johnson reports that among 43 cases of pulmonary embolism found at necropsy, only 3 had given a typical clinical picture, and concludes that pulmonary

embolism should be considered as probable in any patient who is not doing well, even though he has not undergone an operation and does not present any signs of infection. Dyspnoea, tachycardia, and cyanosis are early and frequent signs; collapse, though often present, may be absent, or be the only sign. There is not any single infallible diagnostic criterion, short of necropsy; the condition may simulate, or be simulated by, coronary thrombosis, broncho-pneumonia, sepsis, and surgical shock.

Johnson, A. S. (1940) *New Engl. J. Med.*, **222**, 793.

Thrombosis

Ligature of Femoral Vein in Amputation

According to J. R. Veal ligature of the femoral vein just distal to the sapheno-femoral junction during amputation of the lower extremity, eliminates the danger of embolism. This report is based on the result of 28 amputations of the thigh in which high ligature of the vein was done. The technique of ligature is quite simple, and takes a few minutes only. If enlarged lymph glands obstruct the exposure of the femoral vein, they must be excised. Ligature of the femoral vein, distal to the saphenous vein, prevents oedema in the stump, which develops when the ligature is proximal to the saphenous vein.

Veal, J. R. (1940) *J. Amer. med. Ass.*, **114**, 1616.

LUNG DISEASES: PULMONARY EMBOLISM

See also Surveys and Abstracts 1939, p. 419.

Treatment

Heparin

R. D. McClure and C. R. Lam employed general heparinization in 8 patients with post-operative pulmonary embolism. All of these cases recovered, though one required a further course when a second infarction occurred 5 days after the termination of the first course. The authors also employed heparin with good results in a case of embolectomy of the popliteal artery, and in association with passive vascular occlusion in a case of probable thrombosis of the posterior tibial artery. It was found convenient to administer the heparin in 2 per cent solution (1,000 units, i.e. 10 mg., are usually added to each 100 c.cm. of saline solution; the unitage here employed was 5 times larger than the original Howell unit, which inhibits the clotting of 1 c.cm. of cat's blood). The saline and heparin mixture is allowed to run into the vein at such a rate that the clotting time of the patient's blood is maintained at about 15 minutes. The rate of flow of the solution may be 25 drops per minute, but this varies greatly from case to case.

McClure, R. D., and Lam, C. R. (1940) *J. Amer. med. Ass.*, **114**, 2085.

LUPUS ERYTHEMATOSUS

See also B.E.M.P., Vol. VIII, p. 244; and Cumulative Supplement, Key No. 1004.

Treatment

Sulphonamide Drugs

J. T. Wilson reports a case of acute lupus erythematosus treated unsuccessfully with sulphanilamide, although the blood level of the drug was often above 10 mg. per c.cm., a concentration generally successful against haemolytic streptococci. The patient developed redness and swelling of both cheeks and the bridge of the nose after severe sunburn. She was successfully treated with a vaccine, but 2 years later the condition relapsed. She was investigated for sensitivity to ultra-violet light and the condition then spread to the rest of the body. She improved considerably after injections of splenic extract. A year later she had a severe relapse with an erythematous oedematous skin, cracked lips, and a swollen tongue. Scattered erythematous pustules also appeared on the trunk, and large pustules formed on the fingers. Biopsy confirmed the diagnosis, and culture from the skin lesions

showed β haemolytic streptococci. Sulphanilamide in doses of 60 g. was given by mouth daily, but the patient did not improve. Finally her general condition became worse, and she died 16 days after the beginning of treatment. Post-mortem examination did not show any sign of tuberculosis, but broncho-pneumonia, acute splenitis, and cloudy swelling of the viscera.

H. W. Barber stated that most cases of lupus erythematosus in Great Britain are due to chronic streptococcal infection, rather than to tuberculosis. Barber has used protosil and sulphapyridine in the treatment of the acute and chronic condition in many cases during the past two and a half years. Rubiazol was given to a few patients when these drugs caused severe reactions. Cases, suspected to be tuberculous in origin, were unaffected by the drugs. Before treating streptococcal cases it was found important to eradicate any accessible foci of infection. After receiving the drug for about 8 to 14 days the patients usually became acutely ill. A rise of temperature, a rash, and even rigors sometimes appeared. Barber considered these symptoms to be due, not to a toxic reaction to the drug, but to the liberation of the latent streptococcal toxins by the sulphanilamide. The drug was discontinued and the symptoms rapidly subsided. The effect on the lesion was on the whole good. Owing to the severity of these reactions the drug must be given with great caution in the treatment of lupus. More than one tablet, three times a day, was rarely given in this series.

Barber, H. W. (1940) *Lancet*, **1**, 583.

Wilson, J. I. (1939) *Arch. Derm. Syph., N.Y.*, **40**, 241.

Acute Lupus Erythematosus Disseminatus

Clinical Picture

A. W. Contratto and S. A. Levine report a case of acute lupus erythematosus disseminatus. It is now commonly realized that this condition is a generalized disease involving many organs which almost invariably runs a subacute or chronic but fatal course during which skin lesions appear on the face. The patient was a 16-year-old girl whose condition, clinically and pathologically, corresponded to what is now called lupus erythematosus disseminatus. Throughout there was a distinct delay in auriculo-ventricular conduction (P-R interval 0.24 to 0.26 seconds); this finding in the early course of the disease before the rash appeared led the authors to diagnose rheumatic fever; delay in conduction time had not previously been reported in this condition.

Treatment

The second point of interest was the attempt to sterilize the patient by means of X-rays. The authors were led to adopt this measure because they had never seen a case of this type of lupus erythematosus in a man and because in all women the condition had occurred between puberty and the menopause, the sex relation had also been pointed out by Baehr (1931). Directly after the third X-ray treatment the temperature fell from 104° to 94° F. in 48 hours; this was the first time for 4 weeks the temperature had been normal and moreover the patient felt and looked better. Shortly after the subsidence of the fever the patient showed clinical evidence of lobar pneumonia and Type III pneumococcus was recovered from the sputum, this illness ended fatally. The authors state their belief that the pneumonia was not part of the underlying condition because it was accompanied by a leucocytosis which had not been present during the previous 6 weeks.

Baehr, G. (1931) *Trans. Ass. Amer. Phys.*, **46**, 87.

Contratto, A. W., and Levine, S. A. (1939) *New Engl. J. Med.*, **221**, 602.

LYMPHATIC GLANDS DISEASES

See also B.F.M.P., Vol. VIII, p. 264; Cumulative Supplement, Key Nos. 1006-1009; and Surveys and Abstracts 1939, p. 420.

Non-Infective Enlargement of Lymphatic Glands

The non-infective enlargements of the lymph nodes are classified by J. M. Ross on the basis of the cellular changes. In an account of the structure of the normal

lymph gland and lymphadenoid tissue generally, stress is laid on the importance of the common ancestral or stem cell in the haemopoietic system which, given the appropriate stimulus, gives rise to the cells normally present. The stimulus for the development of the myelocyte is in the bone marrow, that for the lymphocyte in the lymphadenoid tissue. An abnormal stimulus, or the action of a normal stimulus in abnormal circumstances produces abnormal numbers or abnormal combinations, of the different cells.

The non-infective enlargements of the lymph glands are divided into the reticuloses—hyperplasia of differentiated or undifferentiated mesenchyma—and primary neoplasms or reticulosarcomas. The reticuloses are divided and subdivided into (1) Medullary: (a) primary, (i) undifferentiated with acute typhoid-like symptoms in children, subacute but very rare in adults, (ii) haemic, the myeloid, lymphocytic, and monocytic leukaemias or leucoses, (iii) fibro-myeloid, Hodgkin's disease; (iv) histiocytic, 'atypical Hodgkin's disease'. (b) metabolic: generalized lipoidosis, Gaucher's disease, Niemann-Pick disease, and primary xanthomatosis. (2) Follicular, lymphoid and fibrillary. (3) Sinus, acute and chronic. Lymphoid follicular reticulosis was described by Brill, Baehr, and Rosenthal (1925) as follicular lymphoblastoma and sensitive to irradiation, but the condition is a distinct entity and not merely radio-sensitive Hodgkin's disease. The acute form of primary sinus reticulosis runs a rapid and fatal course, with jaundice and anaemia.

Brill, N. I., Baehr, G., and Rosenthal, N. (1925) *J. Amer. med. Ass.*, **84**, 668.

Ross, J. M. (1939) *Brit. med. J.*, **2**, 1029.

New Growths

Follicular Lymphoblastoma

B. Sherwin and M. Spirtes reported a case of follicular lymphoblastoma occurring in a woman aged 57 years. The patient had pain in the left lower chest which she attributed to pleurisy. Examination showed a large mass in the left upper abdomen with leucopenia and a lymphocytosis. Laparotomy showed the mass to be a greatly enlarged spleen which was removed. Some enlarged lymph nodes were also removed. Microscopical examination was made of these specimens and the condition of follicular lymphoblastoma was found. The patient received post-operative irradiation to her enlarged glands. In spite of this she developed gingivitis and fresh groups of glands continued to enlarge. Finally, just over 2 years after operation, the patient died. The authors discussed the pathology of the condition and its relation to the leukaemias and lymphoblastomas.

Sherwin, B., and Spirtes, M. (1940) *Ann. Surg.*, **111**, 459.

LYMPHATIC VESSELS, DISEASES AND INJURIES

See also B1 M.P., Vol. VIII, p. 278, and Surveys and Abstracts 1939, p. 421.

Primary Non-Inflammatory Lymphatic Obstruction

Lymphoedema

H. B. Macey described a case of lymphoedema of the arm which was successfully treated by plastic surgery. The condition occurred in a child of 7 years and was due to a congenital haemangiolymphangioma of the arm and shoulder. Massive oedema deformed the hand and arm and thrombosed veins were on the point of breaking down in the middle and lower parts of the arm. It is no longer considered necessary to establish a communication between the deep and superficial lymphatics in order to drain the affected area. The lymph will drain away into the lymphatics of the muscles if the lymphoedematous tissue is removed. A split skin graft is taken and placed on the muscles beneath the subcutaneous lymphoedematous tissue. This is then sutured over and left for two weeks. At the end of that time the graft has taken and the lymphoedematous tissue can be removed. The limb should be adequately supported after the operation. This procedure was carried out with success in the reported case.

Macey, H. B. (1940) *Proc. Mayo Clin.*, **15**, 49.

LYMPHOPATHIA VENEREUM

See also B.I.M.P., Vol. VIII, p. 287, Surveys and Abstracts 1939, pp. 155 and 421; and p. 92 of this volume

Morbid Anatomy

Bony Changes

L. T. Wright and M. Logan reported 3 cases of lymphopathia venereum with associated bony changes. Although joint affections are fairly common in this condition, bony changes are rare, and before such a diagnosis is made the Frei test must be positive, X-ray examination must show lesions in the bones, and tuberculous, syphilitic, and malignant changes in the bones must be ruled out. In 2 cases there was necrosis of the pelvic bones. Infection was possibly direct from the genital area. In the third case there was a destructive lesion in the spine, but, though the patient was also tuberculous and syphilitic, the bony lesion did not respond to treatment of these infections and was therefore presumed to be due to lymphopathia venereum. The bone disease may be due to direct extension or possibly to haemic infection.

Wright, L. T., and Logan, M. (1939) *Arch. Surg., Chicago*, **39**, 108.

Clinical Picture

Simultaneous Enlargement of Cervical and Inguinal Glands

M. J. Costello and J. A. Cohen report a case of proved lymphopathia venereum with simultaneous enlargement of the cervical and inguinal glands. The cervical buboes were thought to be due to an initial lesion rather than to involvement of the cervical glands as part of the generalized dissemination of the virus.

Elephantiasis of Lips and of Penis and Scrotum

E. W. Netherton and G. H. Curtis report 2 cases of the rare type of hypertrophy of the lips described by Fournier under the name of diffuse hypertrophic syphiloma, and also a case of elephantiasis of the penis and scrotum in which the probable cause was lymphogranuloma venereum. Although it was not possible to make a biopsy of the lesions, and a Frei test was not carried out, the authors seriously doubt the syphilitic origin of Fournier's diffuse hypertrophic syphiloma, and suspect that this condition may be caused by lymphogranuloma venereum. The clinical characteristics of diffuse hypertrophic syphiloma and of lymphogranulomatous elephantiasis of the penis and scrotum were similar.

Costello, M. J., and Cohen, J. A. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 557.

Netherton, E. W., and Curtis, G. H. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 11.

Treatment

Sulphanilamide

A. W. M. Marino *et al.* state that sulphanilamide is very effective in the treatment of the ano-recto-colonic and inguinal manifestations of lymphopathia venereum, and that the effect of the drug is not pronounced on the inflammatory and suppurative phases of the disease. They advise intensive sulphanilamide therapy during the initial period of treatment. A concentration of 5 mg. or more of free sulphanilamide per 100 c.cm. of blood appears to be necessary. A minimum of 24 g. of the drug should be administered over a period of 4 days. After this 3 g. of the drug should be given daily for about 3 months.

Sulphapyridine

K. V. Earle reported the results obtained with sulphapyridine in 12 cases of lymphopathia venereum. Two of the patients suffered from rectal stenosis and 10 from lymphogranuloma inguinale. Earle also treated successfully other cases not reported in this series. The optimal dosage was found to be 0.5 g., 5 to 6 times a day, for 5 days. The dose might be reduced if unpleasant toxic symptoms occurred. Three or 4 days were allowed to elapse, then another course might be given, if necessary, followed by further rests and periods of treatment, depending on the

progress of the disease. The drug acted best if given during the stage of adenitis. If fistulae were present, the treatment was not so successful, and took longer, probably because of infection with 'rough' secondary invaders which were resistant to the drug. Later stages of the disease accompanied by fibrosis or elephantiasis were much more difficult to treat successfully. The author suggested that sulphapyridine might be given as a prophylactic to female carriers living in brothels. These women have a positive Frei reaction, but no clinical signs of the condition, and they are an important focus of infection in tropical regions

Filtrate from Infected Glands

S. Zahawi and F. Akrawi, in a search for some more specific therapeutic agent for lymphopathia venereum, prepared a filtrate from the infected glands as follows. As much blood and pus as could be collected from the glands was inoculated into glucose broth and incubated at 37° C. for 3 to 5 days. It was then passed through a Seitz filter to remove gross particles and contaminating bacteria. After bacteriological tests on laboratory animals had shown it to be sterile, it was applied on dressings twice a day to the incised glands. In some cases 1 to 2 c cm. was injected into the lips of the incision, on the second or third day after this treatment the wound became clear, tenderness and oedema disappeared, very little exudate was left, the general appearance of the ulcer improved, and granulation tissue developed in the first week. Patients generally recovered in from 16 to 21 days

X-rays

J. J. Martin and A. A. de Lorimier employed X-irradiation in 61 cases of lymphogranuloma venereum. In one case only was the patient a female. In all but 4 cases the active process concerned the inguinal glands, one case affected chiefly the tongue and mucosa of the cheek and oro-pharynx, the other 3 were manifested by constrictions in the lower colon and rectum. The initial doses of X-rays should be small, only 50 or 100 r, and the application of the irradiation must be at intervals, over a period of 1 to 3 months. Most of the cases in this series required a total of 1,200 to 1,500 r.

Earle, K. V. (1939) *Lancet*, **2**, 1265

Marino, A. W. M., Turell, R., Buda, A. M., and Nerb, I. (1939)
Amer. J. Surg., **46**, 343

Martin, J. J., and de Lorimier, A. A. (1939) *Amer. J. Roentgenol.*
42, 376.

Zahawi, S., and Akrawi, F. (1940) *J. trop. Med. (Hyg.)*, **43**, 67

MALARIA

See also B.I.M.P., Vol. VIII, p. 304, Cumulative Supplement, Key Nos. 1018 and 1019; Surveys and Abstracts 1939, pp. 142 and 423, and p. 75 of this volume

Clinical Picture

In Children

C. D. Williams describes four types of malaria in children: (i) acute malaria with parasites present, and distinct symptoms; (ii) chronic malaria with parasites present; (iii) chronic malaise in children from a malarial country in whom no parasites can be found, but who improve under adequate treatment with quinine, and (iv) the presence of malarial parasites in the blood of children apparently normal and healthy in every way. The manifestations of malaria are just as various in infants and children as in adults, but anaemia and convulsions are more common, more sudden, and more severe than in adults. Treatment with quinine and iron was advocated, quinine sulphate being preferable to the hydrochloride for oral administration. If gastro-intestinal disturbances hinder absorption of quinine, intramuscular injections are of value. Attacks of fever in babies aged 6 to 18 months are common in malarious countries, immunity is gradually developed, if the patient survives.

Williams, C. D. (1940) *Lancet*, **1**, 441.

Differential Diagnosis

Acute Surgical Abdominal Diseases

R. A. Daniel reported 9 cases of malaria which simulated acute abdominal disease. Five of the patients were males and 4 females, 8 were adults and 1 was a child of 15 years. The pain was sudden in 6 patients. All the patients were nauseated and in 8 of them vomiting occurred. Three patients had had previous attacks of abdominal pain. The abdominal wall was rigid in 3 cases. Two of the patients gave past histories of malaria for which they had received inadequate treatment. The diagnosis was established in 8 cases by the presence of a leucopenia, or its presence when the temperature began to rise. Malarial parasites were demonstrated in the blood of 2 patients. Daniel stressed the importance of blood examination in these cases. The finding of malaria in these patients does not, of course, exclude the possibility of abdominal disease also being present.

Daniel, R. A., Jr. (1940) *Ann. Surg.*, **111**, 436

Treatment

Curative

Simple technique for intravenous quinine - R. K. De describes a simple technique for giving quinine with saline intravenously. The saline infusion is commenced, and while it is flowing the dose of quinine dissolved in 1 or 2 c cm. of distilled water, contained in a syringe, is injected through the rubber tube connecting the saline reservoir and the intravenous needle, thus mixing with saline. Advantages claimed for this method are: the quinine administration can be stopped at the slightest sign of quinine shock, and any intravenous cardiac or respiratory stimulant can be given in the same way; it prevents loss of quinine which may occur if the drug is mixed with the saline in the reservoir, and subsequently the total amount of prepared saline is not employed. Many cases of choleraic malaria come for attention at such a late stage that saline infusion is advisable without waiting for laboratory diagnosis. While the saline is being given a blood slide may be examined and, if this is positive, the quinine can then be given.

De, R. K. (1939) *Indian med. Gaz.*, **74**, 740

Malaria Therapy

Effect of Sodium Bismuth Thioglycollate

L. A. Brunsting and W. R. Love discussed the pyrexial treatment of neurosyphilis by the induction of malaria. They used benign tertian malaria and ideally produced about 12 bouts of fever, each bout occurring on alternate days. Unfortunately, the malaria does not always act true to type. Perhaps a paroxysm may occur every day, or a prolonged paroxysm lasting for days which exhausts the patient may occur. Quinine is unsatisfactory in the treatment of these conditions as it may abort the attack altogether or lead to low irregular fevers. Sodium bismuth thioglycollate given intramuscularly in doses of 0.1 to 0.2 g., produces a temporary interruption in the regular sequence of the malarial paroxysms. The authors used it successfully in 33 cases. The best time for the injection appears to be when the temperature is rising or is near the peak of its elevation. The drug cannot be used instead of quinine to end the malarial infection. In 2 patients an attempt was made to use it, but the paroxysms returned as soon as the drug was stopped. With the help of this drug malarial paroxysms can be used in the treatment of neurosyphilis in patients, such as those with cardiovascular lesions or secondary anaemia, for whom the bouts of uncontrolled fever might prove too exhausting.

Brunsting, L. A., and Love, W. R. (1940) *Proc. Mayo Clin.*, **15**, 285.

MALINGERING

See also B.E.M.P., Vol. VIII, p. 354; and Cumulative Supplement, Key No. 1020.

Feigned Epilepsy in Wartime

R. Ironside gives an account of the diagnosis of feigned epilepsy in war-time. Many methods may be used to simulate the fit, such as putting soap in the mouth

to produce 'foaming' and taking large doses of barbiturates to produce post-epileptic coma. The diagnosis of true epilepsy is not always easy. If it is possible to obtain an electroencephalogram, typical changes will always be seen during or after the fit. Apart from this, such signs as scars on the tongue, incontinence of urine, and subconjunctival haemorrhages must be relied upon. Feigned epilepsy must be differentiated from status epilepticus, head injury, and hysteria, the last-mentioned being particularly difficult. Suspicion should be aroused about the alleged epileptic who attends a new doctor with his fit, who has not previously had fits, and whose history contains discrepancies and contradictions. Relatives or friends should never be present at the examination and in taking a case history separate information must always be obtained from an eye-witness of the fit, or from someone with knowledge of the individual's past history. Over-elaboration of the history should arouse suspicion, such as the assertion of familial or fatal epilepsy, as the familial incidence is very unusual and death from epilepsy very rare indeed, and, when it does occur, is usually in those more than 60 years of age. If there is any doubt in the doctor's mind about a man whom he has not seen before, a certificate of unfitness for service should not be given until the patient's regular practitioner has been consulted.

Ironside, R. (1940) *Brit. med. J.*, **1**, 703

MEASLES

See also B F M P., Vol. VIII, p. 412, Cumulative Supplement, Key No. 1027, and Surveys and Abstracts 1939, pp. 77 and 424

Pathology and Morbid Anatomy

Giant Cells in Prodromal Stage

W. A. Stryker reports the case of a child, 2½ years old, who died of pneumonia and in whom multinucleated giant cells were found in the pulmonary alveoli, the bronchi, the sinuses, the medullary cords of the tracheo-bronchial lymph nodes, the lumina and walls of the bronchial mucous glands, the interstitial connective tissues about the lymph nodes and mucous glands, the spleen, and the lymphatic tissues of the ileum. These cells appeared morphologically similar to those described as specific for the prodromal stage of measles. A history of a possible contact with measles was obtained. It is suggested that disseminated giant cells appear in the prodromal stage of measles.

Stryker, W. A. (1940) *Amer. J. Dis. Child.*, **59**, 468

MEDICO-LEGAL EXAMINATIONS AND REPORTS

See also B F M P., Vol. VIII, p. 453, Cumulative Supplement, Key No. 1030, and Surveys and Abstracts 1939, p. 426.

Blood on Nail Parings

D. P. Lambert reports on the medico-legal value of the finding of blood on nail parings. It had been stated before the Lahore High Court that the detection of human blood on the nail parings of an accused person had absolutely no medico-legal value. The author examined 600 separate nail parings from prisoners, 3 gave a positive reaction and 6 a positive trace with the benzidine test, the remaining 591 being negative. As regards the nails of hospital patients it was found that, assuming that no gross contamination took place after admission to hospital, blood persisted under the nails of these persons for an average of 24 days, with a maximal period of 35 days. It was also found that, if ordinarily clean scissors are used, and reasonable care taken in paring the nails, it seems unlikely that serious contamination can arise from that source. It was concluded that contamination of the nails with blood is neither a common nor a usual finding, and that

contamination of many nails is only likely to occur by contact with shed blood. Although the detection of blood on an accused's nail parings is certainly not conclusive evidence of guilt, it is equally unscientific to say that such evidence is of no value whatsoever

I ambert, D. P. (1939) *Indian med. Gaz.*, **74**, 744

MEGACOLON AND ANAL ACHALASIA

See also B.E.M.P., Vol. VIII, p. 470; Cumulative Supplement, Key No. 1031; and Surveys and Abstracts 1939, p. 426

Megacolon

Treatment

Acetyl-β-methylcholine bromide—J. I. Law employed acetyl-β-methylcholine bromide and liquid paraffin in 6 children with megacolon with complete success. Enemas were given once or twice a day for several days to get rid of faecal concretions and gaseous distension; $\frac{1}{2}$ to 1 fluid ounce of liquid paraffin was also given by mouth each night. The initial dose of acetyl-β-methylcholine bromide was from 0.1 to 0.2 g., by mouth, from $\frac{1}{2}$ to 1 hour after breakfast, increased in 2 or 3 days to 0.2 g. In a few more days the dose might be increased by the addition of from 0.1 to 0.2 g. in mid-afternoon. If diarrhoea occurred, the afternoon dose was omitted. When the dosage was found which produced 1 or 2 stools a day, the patient was discharged, generally taking 0.2 g. each morning, $\frac{1}{2}$ hour after breakfast, and from 1 to 2 teaspoonfuls of liquid paraffin each evening, with instructions to use an enema if distension or constipation occurred. In 2 cases, after several months of this treatment, it was possible to omit all medication with the exception of liquid paraffin.

Acetylcholine as diagnostic test of utility of sympathectomy—G. de Takats employed acetylcholine as a diagnostic test of the utility of sympathectomy in cases of congenital megacolon. The author had previously shown that, while some cases show marked muscular hypertrophy, others have extreme thinning of the colonic wall and a complete loss of musculature. In the latter type of case no form of sympathectomy can help. The use of spinal anaesthesia to inhibit the sympathetic outflow to the colon and so demonstrate the evacuation of the colon had been employed. Since spinal anaesthesia is not always easy to perform, the author stimulated the pelvic parasympathetic outflow, instead of inhibiting the sympathetics. This he effected by injecting 0.075 g. of acetylcholine bromide, which produced a prompt evacuation of a barium enema, if muscular power was available. Following slow instillation of the barium sulphate mixed with equal parts of paraffin-agar, the first radiograph is taken. A second radiograph is taken 45 minutes after subcutaneous injection of the drug. The drug is also useful for evacuating the residual barium sulphate, and for preparing the colon for operation.

de Takats, G. (1939) *Surg. Gynec. Obstet.*, **69**, 762

Law, J. I. (1940) *J. Amer. med. Ass.*, **114**, 2537

MENINGITIS

See also B.E.M.P., Vol. VIII, p. 495; Cumulative Supplement, Key Nos. 1033-1040, and Surveys and Abstracts 1939, pp. 125 and 426

Pneumococcal Meningitis

Treatment

Sulphonamide compounds—J. V. Cable stated that before the introduction of sulphapyridine pneumococcal meningitis was almost always fatal, although a few cases of spontaneous recovery had been reported from America. Thirty-nine cases admitted to the Dudley Road Hospital, Birmingham, were fatal within a week, 23 of them being dead within 3 days. Broncho-pneumonia, lobar pneumonia, and otitis media were the common accompaniments to the meningitis. Cable reported a case occurring in a girl of 7 in whom there were no apparent lesions in the ears.

or chest, who recovered after treatment with sulphapyridine. She received in all 25 c.cm. intramuscularly and a few grains by mouth which had to be stopped in the first instance because of vomiting. The drug caused the temperature to fall almost at once, though there was a slight secondary rise probably due to the formation of an abscess at the site of injection. The general symptoms did not respond so rapidly as the temperature, possibly because the exudate of pneumococcal meningitis is very viscid and takes some time to absorb. By the fifth day of treatment the cerebrospinal fluid was clear and on the tenth day the child was well and mentally bright, and she has remained well. Cable stressed the importance of giving the intramuscular injection deeply, to prevent the formation of an abscess in the subcutaneous tissues.

F. H. Mackay and I. F. Hurteau report the successful treatment by sulphapyridine of 4 cases of pneumococcal meningitis, one of whom received 375 g. during 50 days. These results confirm the hope that sulphapyridine is effective in combating a disease formerly almost uniformly fatal. In one patient only were major toxic effects observed, namely renal complications, haematuria, oliguria, nitrogen retention, hypertension, oedema, and abdominal pain suggesting renal calculi. A more rapid and complete response may be expected when specific serum is used in addition to sulphapyridine than when the latter is used alone. The efficiency of the drug depends on the maintenance of high blood and cerebrospinal fluid levels. To ensure that the blood level of the drug is sufficiently high, frequent blood and cerebrospinal fluid concentration determinations are essential to indicate future doses. Administration of the drug cannot safely be stopped in less than 2 weeks after the temperature and the cell count in the cerebrospinal fluid have become normal.

S. T. Falla treated with sulphapyridine 2 cases of pneumococcal meningitis, with recovery in 1. One child, aged 7 years, received by injection 1 g. of soluble sulphapyridine every hour for 24 hours, then 3 g. every 4 hours. The patient improved somewhat and the dose was repeated on the third day every hour for 12 doses. It was stopped on the morning of the fifth day after a total of 48 g. had been given. The patient continued to improve until the ninth day when he had a relapse. He was again given 1 g. doses of sulphapyridine until a total of 20 g. had been given. The patient then recovered and left the hospital well after 5 weeks. The second patient, a boy aged 10 years, died after 20 hours in hospital although sulphapyridine 1 g. had been given every hour from 1 hour after admission. Falla considered that huge doses of the drug are necessary and justified in the early stages. Since the condition is so dangerous the chance of producing toxic reactions is of secondary importance. It is best to use the soluble form of sulphapyridine either by intravenous or intramuscular injection.

A. M. Grossman reported a case of pneumococcal meningitis in an infant of 3 months of age, who recovered after treatment with sulphapyridine. Type XIV pneumococcus was identified in the cerebrospinal fluid. Treatment consisted of $3\frac{1}{2}$ grams of the drug by mouth, every 4 hours, until the spinal fluid culture was reported sterile. The patient was also given a blood transfusion and 20,000 units of Type XIV antiserum in 150 c.cm. of physiological saline. The patient was discharged after 11 weeks.

D. H. Sherman described a case of pneumococcal meningitis in a boy of $8\frac{1}{2}$ years who recovered on treatment with sulphapyridine. The total dosage of the drug was 130.5 g., the average dose by mouth being 1.0, 1.5 to 2 g., at 4-hourly intervals, day and night. The child also received immune rabbit serum. The cerebrospinal fluid became sterile the fourth day after specific treatment was begun. On this day, a spinal block was diagnosed, inasmuch as only 5 c.cm. of fluid was obtained by lumbar puncture, while 96 c.cm. was recovered by cisternal puncture. On injection of 90 c.cm. of air by lumbar puncture, the block was relieved. This procedure was later repeated 4 times, the pressure of introduction being very slight. The patient was also transfused 3 times.

H. L. Hodes *et al.* treated 6 patients suffering from pneumococcal meningitis with sulphapyridine by mouth, and 11 more patients with sulphapyridine by mouth and its sodium salt intravenously. The drug was given by mouth in doses from 1 to 12 g. every 24 hours, according to the condition of the patient and the concentration of the drug in the blood and spinal fluid. Treatment was continued until the temperature had been normal for 1 week. The dosage was then halved for several days, and the treatment then discontinued. In addition to the oral

administration of sulphapyridine, a 5 per cent solution of the sodium salt was given intravenously to the second group in doses of 0.1 g. per kilogram of body weight every 6 hours until the patient improved and the lumbar puncture was sterile. It was then gradually discontinued. The drug given by mouth was absorbed irregularly and a better concentration was obtained by the intravenous method. The level in the spinal fluid should be 10 to 15 mg. per 100 c.cm. Eight of the 17 patients recovered completely, and of the remaining 9, 4 died within 24 hours of admission to hospital. Some toxic symptoms occurred including agranulocytosis and haematuria. The latter was found to be due to the formation of small calculi. There were no deaths from toxicity of the drug in this series. It was concluded that the use of sulphapyridine and its sodium salt greatly improves the prognosis in pneumococcal meningitis.

Sulphapyridine and serum—S. Vukov successfully treated a case of pneumococcal meningitis by the intravenous injection of specific antiserum together with the oral administration of sulphapyridine. Examination proved the case to be a Type XI infection. On obtaining this information the patient, a child of 5 years of age, was given 5 grains of sulphapyridine with an equal dose of sodium bicarbonate, every 4 hours. Specific antiserum was given in doses of 2 c.cm., 10 c.cm. (60,000 units) being given over a period of 6 hours. After the antiserum there was an almost immediate improvement, and the temperature began to fall. Three days later the child's condition again deteriorated, and a further 60,000 units of serum were given. The temperature then gradually fell to normal, and the child recovered.

Cable, J. V. (1939) *Lancet*, **2**, 73.

Falla, S. T. (1940) *Brit. med. J.*, **1**, 804.

Grossman, A. M. (1940) *Arch. Pediat.*, **57**, 355.

Hodes, H. L., Gimbel, H. S., and Burnett, G. W. (1939) *J. Amer. med. Ass.*, **113**, 1614.

MacKay, F. H., and Hurteau, E. E. (1940) *Canad. med. Ass. J.*, **42**, 463.

Sherman, D. H. (1940) *Arch. Pediat.*, **57**, 112.

Vukov, S. (1940) *Northw. Med., Seattle*, **39**, 221.

Recurrent Pneumococcal Meningitis

After Fracture of the Skull

Sulphonamide therapy. A. R. Elvidge and E. Roseman publish the case of a man, aged 33, who sustained a compound comminuted depressed fracture of the skull opening up the frontal-ethmoidal sinuses on May 23, 1939, and was given sulphapyridine at once prophylactically, but 2 days later meningitis, due to type XXIII pneumococcus, supervened; after treatment he improved, but symptoms returned on June 18, and again, after improvement on July 26, follicular tonsillitis occurred 2 days later. The patient was extensively treated, he received 3,598 grains (225.5 g.) of sulphapyridine, 400,000 units of Type XXIII antipneumococcal rabbit serum and 118 lumbar punctures. In the first attack he had large doses of sulphapyridine and specific serum, in the second sulphapyridine without serum because organisms were not found in the cerebrospinal fluid, and in the third, large quantities of serum and minimal doses of sulphapyridine. Forced drainage (5,000 to 7,000 c.cm. with lumbar puncture daily) was carried on throughout. This case is thought to show the importance of combined and intensive treatment.

Elvidge, A. R., and Roseman, E. (1940) *Canad. med. Ass. J.*, **42**, 460.

Influenzal Meningitis

Treatment

Sulphapyridine—J. Sakula reported a case of meningitis due to Pfeiffer's bacillus which was successfully treated with sulphapyridine. This condition is usually fatal. The patient was a girl of 2½ years presenting most of the classical signs of meningitis. Examination of the cerebrospinal fluid revealed many polymorphs and *Haemophilus influenzae* was cultured from it. The patient was given 2 g. of sulphapyridine, then 2.5 g. for 7 days. The drug was then stopped because of a toxic reaction. The symptoms and signs of the meningitis, however, returned.

On the seventeenth day the drug was therefore resumed for another 5 days. On the twenty-fifth day the patient was much better but by the twenty-seventh she was ill again. The cerebrospinal fluid was normal and she had no specific signs of a return of the meningitis. Blood examination, however, showed a granulopenia which was successfully treated with pentnucleotide and the patient made a good recovery. Sakula stated that large doses of sulphapyridine must be given in this condition. When giving it to children, it is particularly important to do frequent blood-counts, as their bone-marrow is very sensitive to toxic reactions which may result in granulocytopenia.

E. H. Roche and J. I. Caughey reported 2 cases of 'influenzal' meningitis which were successfully treated with sulphapyridine. The first occurred in a boy aged 17 months. Treatment was begun on the second day and continued until the thirteenth day. The total dose of the drug was 18 g. Lumbar puncture was done daily for 3 days and twice more for diagnostic purposes. On the sixth day of the illness it was sterile and the patient made an uninterrupted recovery. The second case was a girl of 12 years who did not receive treatment until the fourth day of the illness. She had a total of 106 g. of sulphapyridine and 6 g. of prosectasine and this treatment was accompanied by lumbar punctures and blood transfusions. On the forty-sixth day of illness the temperature, pulse-rate, and cerebrospinal fluid were normal and the patient made a complete recovery. On one occasion this patient was given human serum into the cerebrospinal fluid to supply complement. Although the series observed was so small, Roche and Caughey concluded that sulphapyridine is a valuable drug in the treatment of 'influenzal' meningitis, because 'influenzal' meningitis has before proved almost invariably fatal.

Chemotherapy unsuccessfully employed - J. C. H. Mackenzie *et al* reported 3 cases of Pfeiffer-bacillus meningitis which were unsuccessfully treated with sulphonamide compounds. In all cases death occurred at the end of 14 days. Necropsy showed the brain of all 3 cases to be distended with pus and much thinned. Petechial haemorrhages also occurred throughout the grey matter. The first case received 24 gr. of prontosil album in 12 days and 2 intrathecal doses of 15 c.cm. of prontosil rubrum. The second child received a total of 78 gr. of sulphanilamide in 17 days and the third 37 gr. of sulphapyridine in 11 days.

Mackenzie, J. C. H., Page, A. P. M., and Ward, L. M. (1940) *Lancet*, **1**, 785.

Roche, E. H., and Caughey, J. I. (1939) *Lancet*, **2**, 635.

Sakula, J. (1940) *Lancet*, **1**, 596.

Tuberculous Meningitis

Diagnosis

Levinson's test - M. Gleich and R. Weintraub compare the results obtained in the diagnosis of tuberculous meningitis by using the Levinson test with those shown alternatively by employing the tryptophane A and B tests. The Levinson test was positive in 100 per cent of these cases and negative in 100 per cent of cases of non-tuberculous meningitis, in which it was used. The tryptophane A test was positive in 89 per cent of tuberculous meningitis cases, but was also positive in 100 per cent of the non-tuberculous cases. The tryptophane B test was positive in 66½ per cent of the tuberculous meningitis cases, but was also positive in 38½ per cent of the non-tuberculous. The results appear to show that the Levinson test is valuable. The test is performed as follows. To 1 test-tube add 1 c.cm. of spinal fluid and 1 c.cm. of 3 per cent sulphosalicylic acid solution, a second test tube contains 1 c.cm. of spinal fluid and 1 c.cm. of 1 per cent mercuric chloride solution. Shake each test-tube well, stopper, and stand at room temperature for 48 hours. Measure the height of the precipitate in each test-tube. The test is positive when the height of the precipitate in the test-tube containing mercuric chloride is twice that of the precipitate in the other tube.

Gleich, M., and Weintraub, R. (1939) *Arch. Pediat.*, **56**, 749.

Benign Lymphocytic Meningitis

C. Armstrong, of the United States Public Health Service, who in collaboration with R. D. Lillie in 1934 isolated the virus of lymphocytic choriomeningitis (acute aseptic or benign lymphocytic meningitis) reviews the infection. This world-wide virus infection is now recognized as responsible for some, but not all, cases described as aseptic or lymphocytic meningitis. Spontaneous infection occurs in white and grey mice, dogs and monkeys, and it is probable that the reservoir for the virus is in mice, not in man. There has been no pathological report on an aetiologicaly proved case, but in a possible case the meninges were infiltrated with lymphocytes and macrophages, the cerebral ventricles dilated, and the choroid plexuses inflamed and partially necrotic. In experimental monkeys and mice the changes were much the same. How the infection passes from infected mice, which excrete the virus in the urine and nasal discharge, is discussed at some length. It may possibly be due to inhalation of dust, and probably not due to the bites of arthropods, for human infections do not occur in June, July and August, months in which arthropods are most active in the northern hemisphere. In answer to the question "Why are there not more human cases?" it is pointed out that at the National Institute of Health examination of about 1,929 sera for the presence of choriomeningitis virus-neutralizing antibodies has shown their presence in between 12 and 13 per cent.; investigation of a considerable sample of these immune persons showed a history of an attack of choriomeningitis to be very exceptional. It is suggested that some, though certainly not all, cases diagnosed as influenza may really be due to infection with the virus of choriomeningitis.

The disease is often preceded by upper respiratory symptoms, and these influenza-like symptoms usually improve but are followed in a few days by sudden severe headache, fever, stiff neck, and other meningitic signs. Recovery is usually complete, though sequelae, probably related to disturbance in the drainage of the cerebrospinal fluid, have been noted in some cases. Diagnosis depends on either injection of the cerebrospinal fluid, or blood, as early as possible in the febrile attack, into susceptible animals, such as white mice or guinea-pigs, or on the demonstration of the development of specific immunity by means of the complement-fixation test which usually becomes available after the tenth day. There is not any specific treatment of proved value. Spinal drainage has often relieved severe headache and vomiting. As a means of prevention mice should be eliminated from dwelling houses.

Armstrong, C. (1940) *Trans. Coll. Phys. Philad.*, 4 ser. **8**, 1.

and Wooley, J. S. (1935) *Publ. Hlth Rep. Wash.*, **50**, 537.

The Chloride Content of the Cerebrospinal Fluid in Meningitis

H. D. Barnes analysed 123 cases, diagnosed as some form of meningitis, among Bantu males mainly between the ages of 15 and 45, in order to determine if there is any relation between the clinical course of meningitis and variations in the chloride content of the cerebrospinal fluid. Numerous analyses showed that there was not any difference between the chloride content of Europeans and of Bantus in normal conditions, and a standard of 700–750 mg. per 100 c.c.m., rather wider than some estimates, was adopted. It is usually agreed that the chloride content in meningitis is diminished, in common with the general tendency of the body fluids, but the relation between chloride depletion and the clinical course has not attracted investigation. There is evidence of an association between reduction of the chloride content and the clinical severity. The probability of death does not appear to be higher in cases with a lower chloride content of the fluid obtained at the first puncture. When chloride values are within normal limits, or, if initially low, the curve rises during subsequent days, the disease is likely to run a mild course, and conversely. The probability of death, however, is not significantly greater if the curve falls within the first few days. The chloride depletion in Addison's disease is mentioned and the possible indication for the adoption in meningitis with a low chloride content of treatment on the same lines as in Addison's disease is thrown out, but not followed up.

Barnes, H. D. (1939) *S. Afr. J. med. Sci.*, **4**, 97.

MENORRHAGIA AND METRORRHAGIA

See also B.E.M.P., Vol. VIII, p. 508; Surveys and Abstracts 1939, p. 430; and p. 20 of this volume.

Meno-Metrorrhagia*Treatment*

Oestriol and Pregneninonol—E. C. Hamblen *et al.* employed oestriol and pregnenonol orally in 7 young women with functional meno-metrorrhagia. This condition was controlled firstly by either curettage or by injections of oestrogenic hormone and progesterone. Oral treatment was begun directly after curettage or when cyclic bleeding had been secured from the injection treatment. Oestradiol was given orally, 4 times daily, in doses of 0.5 mg. (600 oral units) for 14 days. This treatment was begun generally at the onset of bleeding, or a few days thereafter, or immediately following curettage. Immediately following these 14 days of treatment, sodium oestriol-glucuronide as a powder, or oestriol-glucuronide in solution, was given orally, 2 to 4 times daily, in individual doses which varied from 10 to 40 mg., and in total daily doses ranging from 3,900 to 1,800 day-oral units. Simultaneously the patient was given pregnenonol orally, 2 to 4 times daily, in individual doses which ranged from 10 to 40 mg. and in total daily doses ranging from 40 to 160 mg. The oestriol glucuronate-pregnenonol therapy lasted from 10 to 14 days and was discontinued when bleeding began. The patients tolerated well the oral administration of as much as 160 mg. of pregnenonol daily for 14 days each month for several months. Bleeding of cyclical character and of normal amount occurred during treatment, and there were no significant alterations in the urinary titres of sodium pregnandiol-glucuronide and of androgens of the patients investigated.

Hamblen, E. C., Powell, N. B., Cuyler, W. K., and Pattee, C. J. (1940) *Endocrinology*, **26**, 201.

MENTAL DEFICIENCY

See also B.E.M.P., Vol. VIII, p. 520; Cumulative Supplement, Key Nos. 1044-1056; and Surveys and Abstracts 1939, p. 431.

Urinary Creatine-Creatinine in Mental Defectives

L. S. Penrose and C. E. M. Pugh report on more than 500 examinations in duplicate of the creatine and creatinine in the early morning urine of nearly 300 male and of 100 female mental defectives on the ordinary institutional diet. For the estimations of creatinine and creatine the micro-method of Folin was used and an autoclave was available for the hydrolysis. Bichromate standard was used in the calorimeter on account of the very large number of estimations and the relative nature of the results. The article first reviews some essential points in the physiology of creatine-creatinine: 98 per cent of the creatine in the body is stored in the muscles, and creatinine is regularly excreted as a product of muscular metabolism. Normal men on an ordinary diet are said not to excrete creatine, though women often do, but not regularly, because they are less active muscularly or have a less stable endocrine balance; children constantly excrete creatine. In nearly all muscular dystrophies and in nervous diseases affecting the muscles there is creatinuria, sometimes in enormous quantities, and associated with a corresponding fall in the excretion of creatinine. The following conclusions were drawn from this research; in muscular dystrophy and diplegia the excretion of creatine is greatly increased at the expense of creatinine, but in hemiplegia the excretion is normal; a raised excretion of creatine occurs in hyperthyroidism, and thyroid treatment gives rise to a relatively high creatinuria; children show high creatinuria and low creatininuria; in cerebellar ataxy and in the condition left by encephalitis epidemica the excretion of creatinine is high; apart from the post-encephalitic state, no abnormality of creatinine-creatinine was apparent in psychotic patients, and this supports the view that in general there is not any association between psychoses and endocrine disorders, for in endocrine dystrophies the creatinine-creatinine results are irregular and varied according to the nature of the endocrine condition. In congenital syphilis there appears to be a slight increase in the excretion of creatine. In mongolism and epilepsy the results were normal.

Penrose, L. S., and Pugh, C. E. M. (1939) *J. ment. Sci.*, **85**, 1151.

Clinical Types*Mongolism*

Function of thyroid and pituitary -C. E. Benda and E. M. Bixby report their observations on the function of the thyroid and pituitary in mongolism. The fasting serum-cholesterol levels of 50 mongols was within normal limits, indicating that the thyroid is not implicated but the value was very high in 5 cretins. The basal metabolic rates of 25 mongols were normal, whereas those of 3 cretins were very low. The fasting blood-sugar was normal in 51 mongols, but a delayed glycaemic response was given to the dextrose-tolerance test by 10 mongoloid patients; this latter factor suggests that pituitary hypofunction is present in mongolism. Because other workers have stated that mongolism represents a racial regression to the mongolian type, blood-group determinations were done on 125 American mongols. The distribution of the groups was the same as that found in the general population, thus militating against this hypothesis.

Arhinencephaly

R. M. Stewart reported a case of arhinencephaly. A male idiot aged 17 years died of tuberculosis. Necropsy showed complete absence of the olfactory bulbs and tracts. The fascia dentata of both sides was also considerably reduced in size. A similar case has been reported by de Jong, but in this instance the fascia dentata and cornu ammonis were increased in size. It is unusual for the rhinencephalon to be highly developed in man since the sense of smell is subsidiary. The case reported shows that, although the olfactory bulbs and tracts may be absent, part of the rhinencephalon, in this case the hippocampal convolutions, may remain normal.

Benda, C. E., and Bixby, E. M. (1939) *Amer. J. Dis. Child.* **58**, 1240.

de Jong (1927) *Z. ges. Neurol. Psychiat.* **108**, 734.

Stewart, R. M. (1939) *J. Neurol. Psychiat.* **11**, 303.

MIGRAINE

See also B. F. M. P., Vol. VIII, p. 604, and Surveys and Abstracts 1939, p. 433.

Aetiology*Tumour in Calcarine Fissure*

O. R. Hyndman reports a case of migraine in a woman aged 30, cured by removal of a small tumour from the calcarine fissure. Severe migrainous headache accompanied by flashes of light, nausea and vomiting, for six years, had become more frequent recently. Examination showed a left homonymous hemianopia, ventriculography was negative, but X-ray examination showed a small area of calcification in the left parietal region. The right occipital lobe was excised, and embedded in the region of the calcarine fissure was found a small haemangioma. The patient has been free from her attacks for the last 2 years. The case shows that the mechanism responsible for idiopathic migraine probably operates within the limits of the cerebrum including its vessels and the leptomeninges.

Hyndman, O. R. (1939) *Arch. Surg., Chicago*, **39**, 104.

Clinical Picture*Associated Hemiparesis*

J. B. Dynes reported the occurrence of migraine associated with hemiparesis and visual disturbance on the opposite side to the headache in both a mother and her daughter. Both patients began to have migraine at 13 years of age. The daughter is stated to have been unaware of the nature of her mother's attacks. The mother's were not related to menstruation and were unaffected by any treatment, but since the cessation of her periods with radium for uterine carcinoma she has had no attack. The daughter relates her attacks to menstruation, since they tend to occur when her periods are irregular. Seen in an attack, an intramuscular injection of 0.5 mg. of ergotamine tartrate prevented the hemianopia and paresis in the daughter, but not the headache, vomiting, and confusion. This patient is now being

treated with ergotamine tartrate and oestrogenic hormone. It is suggested that the aetiological factors in these two cases are probably endocrine or vasomotor

Dynes, J. B. (1939) *Brit. med. J.*, **2**, 446

Treatment

In Males

Sex hormone therapy—C. W. Dunn reports that oestradiol benzoate in doses from 2,000 R U aborts an attack of migraine if given at the onset. A short series of injections of 5,000 R U of oestradiol benzoate prevents recurrence of attacks for 3 months in patients subject to frequent attacks. A full therapeutic dose of testosterone propionate, 25 mg, does not relieve or influence migraine in males, but in the presence of hypogonadism, it benefits them constitutionally.

Ergotamine Tartrate

Cardiac manifestations—J. B. Carter reported severe cardiac manifestations following the intramuscular injection of 0.5 mg. of ergotamine tartrate for migraine. Immediately after the injection, there occurred palpitation, tachycardia, severe substernal distress, and precordial pain with tightness in the throat. The headache was unrelieved.

Concentrated Oxygen

A. Koffler points out that pure oxygen, as suggested by Alvarez (1939) for the treatment of migraine, can conveniently be given by the ordinary apparatus for estimation of the basal metabolic rate. The apparatus is arranged as for testing the basal metabolic rate except that the kymograph and recording device are not started. The oxygen bell is watched and refilled as necessary.

Vitamin B₁ Therapy

P. Bandler cured 4 cases of migraine by 6 to 9 injections of vitamin B₁. The symptoms observed in cases of migraine certainly are similar to those observed in the typical hypovitaminosis B₁, beri-beri. Besides nervous symptom intense gastrointestinal disturbance was observed in both affections. Whilst beri-beri is a rare disease in Europe, deficiency of B₁ vitamin may arise quite often under physiological conditions such as during growth and pregnancy as well as in diseases such as hyperthyroidism and intestinal affections. In such a case the quantity of vitamin B₁ taken in the food is not sufficient.

Between Attacks

Induced menopause—From analysis of 42 women with migraine who had undergone oophorectomy or hysterectomy, complete or partial, or a sterilizing dose of radium or X-rays, W. C. Alvarez (1940) found that 6 only were cured of migraine, and 5 of the 6 had been treated by radium, in 5 other cases the headaches were milder, in 16 unchanged or better for a time, and in 15 worse. Out of the 12 women treated by radium 3 were worse. At the time the above cases were collected, 3 more patients were met with in whom migraine began after an induced menopause. Migraine often disappears after the natural menopause, but it does not seem that patients should submit to a mutilating operation for the cure of migraine.

Alvarez, W. C. (1939) *Proc. Mayo Clin.*, **14**, 173.

(1940) *ibid.*, **15**, 380.

Bandler, P. (1940) *Schweiz. med. Wschr.*, **70**, 190.

Carter, J. B. (1940) *J. Amer. med. Ass.*, **114**, 2298.

Dunn, C. W. (1939) *Trans. Coll. Phys. Phila.*, 4 ser. **7**, 260.

Koffler, A. (1940) *J. Amer. med. Ass.*, **114**, 1744.

MOTOR NEURONE DISEASE

See also B.E.M.P., Vol. VIII, p. 611.

Clinical Picture

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis is usually progressive and most often is not seen by the neurologist until it is advanced, because the early symptoms are usually

insignificant. I. S. Wechsler states that the condition has not, so far as he is aware, ever yielded to treatment. He therefore publishes 2 cases of recovery after treatment with vitamin E. The first patient was given 3 mg. of ephynal 3 times a day. The weakness in his hands began to clear up and after some weeks of treatment he had good power in his hand and the wasted muscles were beginning to fill out. When the drug was stopped for a few days during treatment the weakness returned. The second patient had symptoms affecting the trunk, tongue, and limbs. She improved on a diet rich in all vitamins with added vitamin B. Later she was given tocopherol acetate, 3 mg. three times a day. After 2 months her condition was practically normal and she is now attending the follow-up clinic of the hospital.

Wechsler, I. S. (1940) *J. Amer. med. Ass.*, **114**, 948.

MOUTH DISEASES

See also B1 M P, Vol. VIII, p. 620; Cumulative Supplement, Key Nos. 1084-1090, and Surveys and Abstracts 1939, p. 434.

Vincent's Angina

Treatment

Nicotinic acid—J. D. King treated 4 severe cases of Vincent's angina successfully with nicotinic acid. The dosage was 250 mg. by mouth for a period of up to 10 days. After 24 to 48 hours pain and ulceration were greatly reduced, the appetite improved, and fusiform bacilli and spirochaetes generally disappeared. Healing of the lesions progressed to cure in every case. The author suggested that Vincent's angina, like pellagra, may be associated with deficient intake or utilization of nicotinic acid and its allied pyridine derivatives of the vitamin B₃ complex.

Iodine potassium iodide mixture—C. Dillon suggested a simple method of treating trench mouth, or Vincent's angina. A paint is prepared by rubbing iodine crystals in a mortar with an excess of potassium iodide, then slowly adding pure glycerin. This is allowed to stand for a few hours, then the excess of iodine and potassium iodide is filtered off. The glycerin solution will contain about 2 per cent of iodine. No water or alcohol should be added. The paint is applied thoroughly with a tooth-brush to the interproximal spaces, then sodium perborate is applied with the same brush and worked into the gingival trough. The paint may also be applied occasionally as a prophylactic measure. It also provides a good dressing for wounds. The author suggested that every soldier should be supplied with a small amount of the mixture and a small package of sodium perborate.

Dillon, C. (1940) *Brit. dent. J.*, **68**, 235.

King, J. D. (1940) *Lancet*, **2**, 32.

Tongue

Leucoplakia

Oestrogenic therapy—I. I. Nathanson and D. B. Weisberger, on the assumption that leucoplakia buccalis and similar lesions were associated with alterations in the menstrual cycle in women, and with a deficiency, or disturbed metabolism, of the sex hormones in both sexes, employed an oestrogen in 38 patients, of whom 25 were women and 13 men. The oestrogenic substance was given in 2 forms, oestradiol benzoate parenterally and α -oestradiol orally. In one group of patients the usual dose of oestradiol benzoate was 10,000 rat units in 1 c.c. of sesame oil every other day for 6 injections. This was supplemented by 0.17 to 1.0 mg. of α -oestradiol orally each day for the same period. In the other group 0.17 to 0.5 mg. of α -oestradiol only was given daily for 90 to 120 days. Complete disappearance of the lesions occurred in 16 cases (42 per cent), marked improvement in 15 (39 per cent), and no change in 7 (19 per cent). The first change noted in the mucosa was oedema and haziness and, in some cases, the leucoplakic membrane could be detached readily from the underlying tissue, leaving a pink smooth surface. In most of the successful cases there was a reappearance of the leucoplakia in 3 to 6 months after the therapy was discontinued. In such cases it was found that a maintenance dose of 0.17 mg. α -oestradiol daily was sufficient to keep recurrences at a minimum.

Black Hairy Tongue

F. H. Diggle reports a case of black hairy tongue in a man aged 59 years. He had been treated by implantation of radium needles and with a radium collar for epithelioma of the left tonsil and left side of the tongue. The growth entirely disappeared, but a few months later a black hairy condition appeared on the tongue just in front of the circumvallate papillae. All known methods of treatment failed and the condition caused the patient much discomfort; he was obliged to remove the hairs each morning with forceps. A small patch, resembling a recurrence of the epithelioma, then appeared on the soft palate. This was treated by implanting radon seeds. One month after this treatment the hair entirely and permanently disappeared from the tongue. It is suggested that it was more than a coincidence that the hairs appeared after one radiation and disappeared after the second.

Potassium chlorate therapy. J. W. Tomb also reports a case of black hairy tongue in which all previous treatment had failed, but which was cured by a mixture containing 5 grains of potassium chlorate, 3 times a day. After taking the mixture for 10 days, the tongue became normal. After 2 weeks' interval the treatment was repeated for another 10 days, and 18 months later there had been no recurrence of the condition.

Carcinoma

G. W. Saleeby reports squamous-celled epidermoid carcinoma of the tongue in a girl aged 15. Under radium and X-ray therapy the primary lesion disappeared, but a cervical metastasis proved to be radio-resistant, and death followed one year after the onset of symptoms. The condition in early life is rare. The author collected 8 cases only of cancer of the tongue in subjects under 20 years of age, and 2 in new-born infants.

Spontaneous Amputation

Partial or complete spontaneous amputation of the tongue is very rare, though any acute or chronic infection can apparently result in this condition. S. Richman reports a case in a man, aged 56, with a very extensive carcinoma involving the major area of the tongue, and infiltrating deeply into its muscles. X-rays and interstitial radium therapy resulted in a temporary recession of the growth. Recurrence, however, advanced very rapidly, and severe haemorrhage from the ulcerated growth necessitated ligation of the external carotid artery on one side. About 4 months later the tongue became soft and fluid-like, and a few days afterwards the whole tongue sloughed off, leaving an irregular necrotic area on the floor of the mouth with a very small portion of tongue protruding in its right posterior region. What parts the irradiation and the ligation of the external carotid played in the separation of the tongue could not be definitely stated. Possibly the carcinomatous ulceration may have resulted in the spontaneous amputation, the fibrosis and vascular thrombosis secondary to the irradiation, and the relative ischaemia due to ligation of the external carotid may have accelerated, or even possibly caused, the condition.

Diggle, F. H. (1940) *J. Laryng.*, **55**, 166.

Nathanson, I. T., and Weisberger, D. B. (1939) *New Engl. J. Med.*, **221**, 556.

Richman, S. (1939) *Amer. J. Roentgenol.*, **42**, 843.

Saleeby, G. W. (1940) *Amer. J. Cancer*, **38**, 257.

Tomb, J. W. (1940) *J. trop. Med. (Hyg.)*, **43**, 155.

Palate*Palatal Myoclonus*

O. Sittig and V. Haskovec consider that palatal myoclonus is usually due to some intracranial vascular accident, either haemorrhage or softening. The lesion may be in the tegmentum of the pons or in the cerebellum involving the dentate nucleus. The lesion involves muscles of both breathing and swallowing, and may be due to a release of the inhibition exercised by the higher centres on the bulbar nuclei. They report the case of a man of 77 years with pseudobulbar paralysis and hemiplegia and myoclonic movements of the palate and pharynx of the same

side. The blood-pressure was 170/80 mm Hg. Necropsy showed a lesion in the right cerebellar hemisphere involving the dentate nucleus and adjacent white matter. There was pseudo-hypertrophy of the left olivary body, with degeneration of the right restiform body and right superior peduncle, and atrophy of the left red nucleus. Other workers have described the same lesion in this condition. Three more cases of clinical pseudobulbar paralysis were reported, 2 with hypertension.

Sittig, O., and Haskovec, V. (1940) *Arch. Neurol. Psychiat., Chicago*, **65**, 413.

Jaws

Median Mental Sinus

G. Duckworth reported a case of median mental sinus, a rare, but characteristic, condition first described by Hamilton Bailey. A woman, aged 31, consulted the author on account of a papule on the point of her chin. This had been present for 7 years, and had resisted all forms of local treatment. It periodically discharged a little purulent fluid. The papule, which was about the size of a split pea and freely movable, was erythematous, its surface was covered by a slight scale, and it was surrounded by a circular patch of marked oedema. The crowns of the lower incisor teeth were in fairly good condition, though some of the teeth were loose. Dental radiographs showed an area of rarefaction round one of the roots of the right lateral incisor tooth, suggesting a large abscess. The offending tooth was removed and within a few days the papule became much less conspicuous. A few weeks later the sinus had healed and the redness was gone. Cases of median mental sinus are often diagnosed as infected sebaceous cysts. Although removal of the affected tooth generally cures the sinus, if it is of fairly recent occurrence, scraping and packing may be necessary in more long standing cases.

Duckworth, G. (1940) *Brit. J. Derm.*, **52**, 57.

MUMPS

See also B. I. M. P., Vol. IX, p. 1; Cumulative Supplement, Key No. 1092, and Surveys and Abstracts 1939, p. 435.

Clinical Picture

Neurological Complications

Opinions differ with regard to the frequency of neurological complications in patients suffering from mumps, but even in cases in which clinical symptoms demonstrating an affection of the nervous system were absent, signs of inflammation were often observed in the cerebrospinal fluid. Different neurological symptoms have been observed as a complication of mumps, such as encephalitis, polyneuritis and meningo-radicularitis. In a case observed by G. Glueck consciousness suddenly became disturbed at a time when mumps was already improving. Intense cerebellar signs developed and the pupils reacted only slowly. Improvement of the neurological symptoms started after two weeks. The diagnosis of encephalitis was given affecting in the first place the cerebellum. Affection of the nervous system possibly began by a haemorrhage into the cerebellum, but this was not supported by examination of the cerebrospinal fluid, as, with the exception of mild lymphocytosis, the cerebrospinal fluid was perfectly normal.

Glueck, G. (1939) *Riv. Neurol.*, **12**, 309.

MUSCLE DISEASES

See also B. I. M. P., Vol. IX, p. 11; Cumulative Supplement, Key Nos. 1093–1099, Surveys and Abstracts 1939, p. 436, and p. 68 of this volume.

New Sign of Mild Paresis

The patient lies down in the horizontal position with the eyes closed, he lifts his arms up to vertical position slowly and keeps them in this position for some seconds. If they were not in the same position the doctor corrects the position.

The patient is then asked to lower his arms slowly. If there is a slight paresis the paretic arm will be lowered somewhat less than the normal one, a difference of 1 to 2 cm. will result regularly. The 'lowering the arm' sign was observed in all cases of organic paresis examined by Fischer. With regard to functional cases nothing definite can be said at present. Malingering is demonstrated if the 'paretic' arm is lowered somewhat more quickly than the normal one.

Organic mild paresis in cerebral affections is demonstrated in this method even if the abdominal reflex is still unaffected.

Fischer, O. (1939) *Schweiz. med. Wschr.*, **69**, 1175.

Injuries

Spontaneous Haemorrhage into Rectus Abdominis

B. M. Black and L. K. Stalker report a case in a man, aged 48, who had 2 attacks of pain and, as exploration subsequently showed, of haemorrhage into the sheath of the right rectus abdominis muscle in its lower third after severe attacks of coughing. The white count was 12,000, 92 per cent being polymorphonuclears. Exploration showed a bleeding branch of the inferior epigastric artery. As appendicitis was the first diagnosis, the appendix was removed, and showed chronic change. The subject is reviewed. Wohlgemuth in 1923 collected 127 cases, and in 1938 R. L. Payne collected 165 more and estimated that twice that number had been observed but not reported. The haemorrhage, which is usually unilateral and below the umbilicus, may occur (i) in persons with healthy muscles and blood vessels and may be ascribed to muscular effort, 107 of Wohlgemuth's 127 were in healthy subjects, (ii) in persons with disease or attenuation of muscles, or (iii) in those with severe arterial disease. The chief importance of the condition is its imitation of intra-abdominal disease. As the haemorrhage may recur, the treatment should be surgical and consist in removal of the clot and ligation of the bleeding vessel.

Black, B. M., and Stalker, L. K. (1940) *Proc. Mayo Clin.* **15**, 206.

Payne, R. L. (1938) *Ann. Surg.*, **108**, 757.

Wohlgemuth, K. (1923) *Arch. klin. Chir.*, **122**, 649.

Ossification of Sternomastoid

G. Carlo and G. Leopoldo described a case of ossification in the sternomastoid muscle in a woman who had no history of injury or disease. The authors reviewed the different possible causes of bone formation, by metastasis, after necrosis and precipitation of calcium, by trauma, and as a manifestation of a generalized disease. They reported marked and rapid results by X-ray therapy, which they attribute to stimulation of absorption of calcium after conversion from an insoluble into a soluble form under the influence of the X-rays.

Carlo, G., and Leopoldo, G. (1939) *Quadr. radiol.*, **17**, 168.

Myositis

Dermato-Myositis

P. A. O'Leary and M. Waisman studying 40 cases of subacute and chronic dermato-myositis, observed at the Mayo Clinic during the past 13 years, found that there was a high incidence of disease before the onset of the condition. Bacteriological studies indicated the possibility of localization of various micro-organisms in muscle. The authors agreed with the hypothesis that the disease might be caused either by bacterial infection from the blood-stream or by toxic action of bacterial products on the muscular and cutaneous structures. The abnormal metabolism of creatine is probably a constant occurrence. Microscopical study of the earliest lesions of muscles indicated that the primary reaction might be manifested by the sarcoplasm rather than by the interstitial cellular infiltration.

O'Leary, P. A., and Waisman, M. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 1001.

Myositis Ossificans Traumatica

A. Thorndike stated that myositis ossificans traumatica is an inflammatory process of muscle in its early stages, and before ossification is actually shown

radiographically. As ossification occurs, this inflammatory process gradually subsides. The ossification is gradually absorbed, sometimes partly and sometimes wholly, depending on its size and location. The muscle function returns to normal, except in cases in which ossification occurs near a joint. Treatment necessitates the immediate application of cold and a compression bandage to control haemorrhage, and later heat to assist absorption of the haematoma. Operative removal of the ossification is indicated only when the latter occurs near a joint in the origin or insertion of a muscle, when joint function is permanently impaired, and then only from 12 to 24 months after the injury.

Thorndike, A. J. (1940) *J. Bone Jt. Surg.*, **22**, 315

Muscular Dystrophies

Physiological Significance of Creatine-Coefficient and Creatine-Tolerance Test

H. H. Beard and E. J. Jacob consider that the creatine coefficient possesses little, if any, physiological significance because muscle creatine is not transformed into urinary creatinine, because there is no relation between creatinine output and body weight, and because the creatinine output depends on the rate of protein catabolism in the body. The physiological significance of creatine tolerance in the myopathies is also questioned (i) because certain muscles of the myopathic patient are unable to utilize exogenous creatine brought to them; (ii) because ingestion of amino-acetic acid causes an increase in metabolic creatine in the muscles with definite clinical improvement in some cases, at the same time causing a decrease in the creatine tolerance; (iii) because wide variations in creatine retention and excretion occur after its ingestion in both normal and myopathic persons; and (iv) because there is a close relation between creatine synthesis and water metabolism, which is not revealed by the creatine tolerance test. A better diagnostic and prognostic test in cases of myopathy is furnished by a study of the excretion of creatine and creatinine before and after ingestion of amino-acetic acid. The disappearance of the creatinuria, with resulting clinical improvement of certain types of disease, shows the ability of the patient to utilize, rather than simply to store or tolerate, the creatine synthesized during the period of treatment.

Treatment

Wheat-germ oil—Experiments have shown that muscular and nervous symptoms developed in rats receiving a diet deficient in vitamin E. It has been suggested that muscular dystrophies, amyotrophic lateral sclerosis, and tabes (which only occurs in some syphilitics) may be due to a deficiency of vitamin E. I. Bicknell stated that degeneration in both the nerves and muscles underlies these conditions. He also found that vitamin E, which, when they are stale, disappears from foods such as milk and butter which normally contain it, is often deficient in the normal diet. The anti-sterility factor in vitamin E is probably not identical with the myotrophic and neurotrophic factors, though they both occur together in wheat-germ oil. Bicknell reported 25 cases of muscular dystrophies and tabes which were treated with vitamin E. Many of them improved even if they were bedridden. One case was cured, but 2 cases of tabes were unaffected by the treatment. He suggested that it might be tried in disseminated sclerosis and as a prophylactic measure against infantile paralysis, to make the anterior-horn cells more resistant. This work suggests that these dystrophies are deficiency diseases which are curable.

S. Stone employed wheat-germ oil in 5 patients with muscular dystrophy following acute poliomyelitis, and in one with muscular atrophy after an attack of multiple neuritis or neuromyeloradiculitis. Definite improvement occurred in cases with muscular dystrophy, improvement being shown by increased muscular strength, the disappearance of fatigue and muscular pain on slight exertion, change in muscle texture, and displacement of dystrophic musculature by normally contracting muscle tissue. In cases of muscular atrophy following involvement of the nervous system, an increase in amount of regeneration of muscle tissue was apparent after the addition of wheat-germ oil to the vitamin B complex the patients were receiving. The dosage was 3 minims (0.2 c.c.m.) of wheat-germ oil, 3 times a day, later increased to 10 minims (0.6 c.c.m.) 3 times a day. The addition of vitamin B complex to vitamin E appeared to increase the therapeutic effectiveness of the latter.

Pseudo-Hypertrophic Muscular Dystrophy

Vitamin B₆.—W. Antopol and C. E. Schotland employed vitamin B₆ (2-methyl-3-hydroxy-4:5-dihydroxymethyl pyridine) in 6 cases of pseudohypertrophic muscular dystrophy with considerable improvement in their condition. Since this vitamin is a newly-synthesized compound, its pharmacological action has not been sufficiently investigated. No untoward effects were observed in any of the patients. The dosage ranged from 100 to 500 mg. weekly given by subcutaneous injection.

Antopol, W., and Schotland, C. F. (1940) *J. Amer. med. Ass.*, **114**, 1058.

Beard, H. H., and Jacob, E. J. (1939) *Arch. Neurol. Psychiat.*, **42**, 67.

Bicknell, F. (1940) *Lancet*, **1**, 10.

Stone, S. (1940) *J. Amer. med. Ass.*, **114**, 2187.

Myotonia Congenita*Diagnosis*

In early infancy.—The diagnosis of myotonia congenita offers great difficulty in early infancy. W. von Kiehl observed a remarkable sign in several quite young patients, one of them only five weeks old. When this infant had a bath and her face was rubbed with a rag downwards both eyes were closed as observed in other infants, but remained closed for several seconds and were opened only quite slowly, as a result of myotonic contracture of eye-muscles. Sometimes one eye was opened before the other, and marked difference was observed in the size of the palpebral fissures when myotonic contracture in one eye subsided before contracture in the other one.

Kiehl, W. von (1939) *Arch. Kinderheilk.*, **118**, 79.

Myotonia Atrophica*Treatment*

Testosterone propionate.—F. H. Hesser *et al.* gave testosterone propionate in doses of 25 mg., intramuscularly every other day for 2 months, in 2 male patients with myotonia atrophica and testicular atrophy. These patients were taking quinine daily for the muscle condition. Within a week of the first injection the grip rapidly became stronger, reached a peak within the next 2 weeks and maintained this higher level. Temporary withdrawal of the drug in one case was followed by decreased dynamometric values within 4 days of the last injection. Both patients welcomed the sense of greatly increased strength and the general constitutional improvement, which was manifested by buoyancy of spirit, feeling of well-being, and lessened fatiguability. Posture and gait improved noticeably.

Hesser, F. H., Langworthy, O. R., and Vest, S. A. (1940) *Endocrinology*, **26**, 241.

Pyramidal Hypertonia*Treatment with Haematoporphyrin*

W. Sterling and W. Stein consider that the usual treatment of muscular hypertonia of pyramidal origin (e.g. neurosurgery, physico-therapy and the use of drugs such as bromine and curare) is not very successful. By chance, when treating a depressed patient with haematoporphyrin, the authors found that there was a regression of spasm and muscular hypertonia. A patient, aged 54 years, suffered (among other things) from paraplegia spastica inferior with pseudo-bulbar symptoms and very painful paroxysmal spasms of the lower extremities. After 3 injections of haematoporphyrin there was a retrocession of the depressive state and after 4 more injections a remarkable regression of the muscular hypertonia. Passive movements, previously impossible, could be made and the patient started to walk again.

The authors then used injections of 0.5 c.c. of 0.2 g. of haematoporphyrin in aqueous solution, giving a total of 10 to 12 injections separated by intervals of 8 hours. They found after 2 or 3 injections that passive movements became possible, immobilized patients improved, and spasmodic crises disappeared. The haemato-

porphyrin treatment is recommended in all those cases in which the muscular hypertonía predominates over the parietic symptoms

Sterling, W., and Stein, W. (1939) *Pr. med.*, **47**, 1287

MYASTHENIA GRAVIS

See also B F M P., Vol. IX, p. 34, Surveys and Abstracts 1939, p. 439; and p. 68 of this volume

Aetiology

Lesions of Thymus

H. G. Miller reviews the published work on the relation of the thymus to myasthenia gravis, and described 5 further cases with necropsies. In 2 cases an encapsulated tumour of the thymus was associated with remnants of normal thymus. In 2 cases there was a persistent thymus, with marked peripheral epithelial hyperplasia in one case. In one case the thymus was not identified. The number of reported cases of myasthenia gravis in which necropsy has been carried out is now 87, in 47 of these, distinct anatomical lesions of the thymus were present. It is suggested that cases of this disease be given careful radiological examination in an effort to diagnose thymic involvement, and that irradiation and surgical removal be tried more often in treatment.

Role of Potassium

J. N. Cumings carried out potassium-balance experiments in 2 cases of myasthenia gravis, and studied the effect of prostigmin on the excretion of potassium. The author had previously (1939) shown that the affected muscles of patients with the disease contained more potassium than normal, and that, after subcutaneous administration of prostigmin to myasthenia patients, the concentration of potassium in their muscles falls to a normal level, while the serum potassium may rise. In the present experiments it was shown that, although the muscles liberated potassium into the blood serum after the injection of prostigmin, there was no increase in urinary excretion of potassium. The potassium appeared to be retained in the blood, and to return to the muscles as the weakness of the latter reappeared.

Cumings, J. N. (1940) *J. Neurol. Psychiat.*, **111**, 115.

Miller, H. G. (1940) *Arch. Path.*, **29**, 212.

Clinical Picture

Relation to Hyperthyroidism

M. W. Thorner reported a case of myasthenia gravis in a woman of 20 years which responded to treatment with prostigmin. Later the patient developed hyperthyroidism with an enlarged thyroid, tachycardia, and a basal metabolic rate of +52 per cent. At the same time the myasthenic symptoms had all but vanished. The patient was treated with irradiation of the thyroid gland and, after 2 months, the basal metabolic rate was ± 19 per cent, the pulse-rate ranged between 90 and 130, and the thyroid gland was smaller. She only needed an occasional tablet of prostigmin at this time. Another patient with uncomplicated myasthenia gravis was given thyroid with a remission of the symptoms. This relation between hyperthyroidism and myasthenia gravis, the one being better when the other is worse, has been observed before and Thorner considers it to be of scientific rather than therapeutic interest.

Thorner, M. W. (1939) *Arch. intern. Med.*, **64**, 330.

Treatment

Evaluation of Various Drugs

N. S. Schlezinger compared the efficacy of various treatments in myasthenia gravis. Seven patients were treated and the results of treatment were compared by means of various tests to find the power and fatigability of the muscles, such as repeated protrusion of the tongue. The first patient was treated with ephedrine with good results. Amino-acetic acid (glycine) therapy was ineffective in this case, but the two drugs together gave even better results than ephedrine alone. The second patient was treated with the same drug with the same results. The third

patient was given amino-acetic acid and also anterior pituitary extract, and both drugs failed. Ephedrine improved the condition, but prostigmin gave the most striking results. The fourth patient received the same drugs, with the exception of amino-acetic acid, as the third, with the same results. The fifth patient was a child of 13 years and in her case prostigmin combined with ephedrine produced better results than prostigmin alone. The treatment of the sixth patient confirmed this observation. It also showed that ephedrine acts mainly on the extremities, whereas prostigmin is more general in its effects. The seventh patient was a rapidly advancing case of myasthenia gravis which responded best to the oral administration of prostigmin and ephedrine, rather than to prostigmin alone. Schlezinger concluded that of all the remedies suggested, this last is the best, provided there are no toxic manifestations.

Prostigmin

H. R. Viets and R. S. Schwab analysed 44 cases of myasthenia gravis treated with prostigmin. The highest incidence occurred in the second and fifth decades. Presenting symptoms varied from ptosis to general weakness and dysphagia. The diagnosis may be made from the history and examination but the prostigmin test is probably the best method. The dosage of prostigmin varied but it is safe to give 20 to 25 tablets of 15 mg. each by mouth during 24 hours. Ephedrine sulphate has been used with success to increase the effect of the drug and guanidine with less success. Potassium chloride is also useful. Of the 44 patients, watched over a period of 5 years, 5 have died and 7 shown full remissions.

Guanidine Hydrochloride

A. S. Minot *et al.* reported 5 cases of myasthenia gravis successfully treated with guanidine hydrochloride. Large doses, up to 250 mg. eight times a day, were given without the production of hyperguanidaemia. If this condition is produced both in normal persons and those suffering from myasthenia gravis it is attended by gastro-intestinal and other toxic symptoms. Atropine relieves these symptoms but the dose of guanidine should be reduced nevertheless. It was not necessary in this series to supplement the treatment with prostigmin, but it can be done. Guanidine alone produced a marked and well-sustained improvement in muscular function. Potassium citrate, in one case, increased the effect of the guanidine and prostigmin.

Minot, A. S., Dodd, K., and Riven, S. S. (1939) *J. Amer. med. Ass.*, **113**, 553.

Schlezinger, N. S. (1940) *Arch. intern. Med.*, **65**, 60.

Viets, H. R., and Schwab, R. S. (1939) *J. Amer. med. Ass.*, **113**, 559.

MYCOSIS FUNGOIDES

See also B. E. M. P., Vol. IX, p. 51.

Aetiology

M. Neithammer, after reviewing the literature on mycosis fungoides, considered that it supported the opinion that the disease had an infective aetiology. He reported a case from the skin lesions of which streptococci were obtained, partly in pure culture. The same strain of streptococcus was obtainable at a university clinic from 2 other cases of mycosis fungoides. Furthermore, the antigens produced with these strains gave positive complement-fixation reactions with serum from 2 cases of the disease, though the strains were not pathogenic for either rabbits or guinea-pigs.

Neithammer, M. (1940), *Arch. Derm. Syph., Wien*, **179**, 484.

MYOPIA

See also B. F. M. P., Vol. IX, p. 66, and Surveys and Abstracts 1939, p. 129.

Treatment

Vitamin D and Calcium

A. A. Knapp suggested that a disturbance of the vitamin-D-calcium-phosphorus metabolism is concerned in the aetiology of myopia. Fifty-three patients were selected for study, their ages varying from 3 to 20 years, and their degree of myopia

ranging from -- 0 25 D to -- 41 D. Vitamin D was given in the form of calciferol, 60 drops daily, with calcium, in tablet form. Results showed that in 66-67 per cent of the patients who carried out this treatment regularly there was either a reduction in their myopia, or the condition did not progress. This therapy may, in those cases which respond, produce an actual shrinkage of both cornea and sclera.

Knapp, A. A. (1939) *Amer. J. Ophthal.* **22**, 1329.

NAILS, DISEASES OF

See also B.E.M.P., Vol. IX, p. 83, and Surveys and Abstracts 1939, p. 441.

Tumours

Subungual Melanoma

In a monograph on subungual melanoma G. I. Pack and F. E. Adair refer to Jonathan Hutchinson's description in 1886 under the title melanotic whitlow 'because it resembles whitlow and is usually so named at first'. It has also been called onychial melanoma, melanotic sarcoma, melanocarcinoma, and melanoblastoma of the nail bed. Among 477 cases of melanoma since 1917 in various parts of the body 16, or 3.4 per cent, were subungual, the average age of these patients from the Memorial Hospital for Cancer and Allied Diseases, New York, was 59 years, as contrasted with 48 years for melanomas of other regions. The average age of 48 cases of subungual melanoma collected from published sources was 56 years. The thumb and the great toe were most often attacked, and the hand more often than the foot. The differential diagnosis was considered from 13 other conditions, paronychia, pyogenic granuloma, onychomycosis nigrescens, subungual haematoma, primary syphilitic chancre of the finger, gangrene of the toe, subungual osteochondroma (Dupuytren's exostosis), subungual fibroma, subungual keratosis, subungual epithelioma, subungual angiosarcoma (Kaposi's disease), subungual tumour of the glomus, and metastatic tumour of the nail bed, the last being a curiosity of which the authors had experience of 2 cases only. The percentage of cure of subungual melanoma after early amputation was higher than for melanoma in other positions. The monograph is provided with an exhaustive list of references.

Pack, G. I., and Adair, F. E. (1939) *Tumours of the Hands and Feet*, London, p. 55.

Onycholysis

D. D. McRoberts described a case of onycholysis, a painless partial separation of the nails without preceding symptoms of systemic or local inflammation. The typical process is separation of the nail, beginning at the free distal end with slow progress of separation towards the lunula, where the nail is generally held securely enough to prevent separation, except by force. The process may begin on single, or several, nails of the fingers or toes. The nails may first become thickened and hard, or this process may occur later during the course of the disease. The space between the nail and nail bed is filled with fine easily removable horny scales and dirt particles. The four factors stated by Viecelli (1936) to be necessary for the disease were present in the author's case. These factors were: traction on the nail, softening and maceration of epidermis under the free edge, due to constant moisture or exposure to chemicals; predisposition or low-grade infection; and over-zealous cleaning.

McRoberts, D. D. (1940) *Northw. Med., Seattle*, **39**, 95.

Viecelli, J. D. (1936) *Arch. Derm. Syph., N.Y.*, **33**, 697.

NARCOSIS, PROLONGED

See also B.E.M.P., Vol. IX, p. 98, Cumulative Supplement, Key No. 1118, and Surveys and Abstracts 1939, p. 442.

Paraldehyde and Dial

M. B. Brody found that 3 fluid drachms of paraldehyde with 3 grains of dial

often produced a long and sound sleep in excited patients, when other powerful narcotics were ineffective. He therefore tried this combination as a means of producing prolonged narcosis in 90 patients, comprising cases of mania, depression, and schizophrenia. The average time out of 24 hours spent fully asleep, drowsy, and awake was 17.2 ± 1.9 hours, 2.0 ± 1.5 hours, and 4.8 ± 2.3 hours, respectively. This amount of sleep was particularly satisfactory because 52 out of the 90 treatments were given to some of the most difficult patients. The normal dose was 1 fl. oz. of a suspension containing 90 minims of paraldehyde and 1 minim of solution of atropine sulphate (1 in 1,000) to 1 fl. oz. The dose of dial, $1\frac{1}{2}$ grains, was crushed into the draught. The first dose of the drug was given $\frac{3}{4}$ hour after breakfast, and this dose was generally repeated in the evening. Some patients required a further dose of the paraldehyde mixture without the dial, during the afternoon or the night. Sometimes the dosage had to be increased for a few days, not more than 3 double doses of the paraldehyde mixture and 2 double doses of dial being given in 24 hours. The most troublesome complication was vomiting; other complications were restlessness, pyrexia, and albuminuria.

Brody, M. B. (1940) *J. ment. Sci.*, **86**, 526.

NEMATODE INFECTIONS, INTESTINAL

See also B. I. M. P., Vol. IX, p. 125, and Cumulative Supplement, Key Nos. 1126-1130.

Oxyuriasis

Treatment

Gentian violet. W. H. Wright and F. J. Brady studied the efficacy of gentian violet in the treatment of pinworm infestation. The parasite is the most commonly found in man in the United States in spite of improved hygiene and more efficient meat inspection. The condition often attacks families and it is useless to treat one person if other members of the family are also infested, because the parasite is so easily transmitted from one to another. The best method of detecting oxyuriasis is by means of the NIH swab. This consists of a glass rod tipped with a small square of cellophane. The tip is stroked over the perianal region and the eggs, if present, generally adhere to the cellophane which may be removed, mounted between a glass slide and coverslip and examined under the microscope for ova. All established treatments for the condition, such as single doses of tetrachlorethylene, are by no means entirely satisfactory. The authors treated 224 patients on a familial basis with gentian violet, and proved this preparation to be superior to all others. The results of treatment were checked with the NIH swab. Adults were given two 32 mg. ($\frac{1}{2}$ grain) tablets of gentian violet 3 times a day before meals. Children were given 10 mg. for each year of apparent age, per day, also divided into 3 doses. The patients were divided into 4 groups. The first contained 107 patients and they received enteric-coated gentian violet tablets for 10 days, 91 per cent of them were cured in from 10 to 21 days after the end of the treatment. In the second group 30 patients received the same tablets for 8 days, were rested for 7 days, and were then treated for a further 8 days; 14 to 21 days after the end of treatment 90 per cent of them gave negative swabs. In the third group 19 patients were treated in the same way and their swabs, taken from the forty-second to the forty-eighth day after treatment, were negative in 58 per cent. Gentian violet tablets with a water-soluble coating were given by the same method to 68 patients in the fourth group. The tablets disintegrate in the small intestine about $4\frac{1}{2}$ hours after they have been given. Of this group 79 per cent had negative swabs on 7 consecutive days 42 and 48 days after the end of treatment. In the whole series there were a few mild toxic reactions which were controlled by reducing the dosage or discontinuing the treatment for a day or two. They included nausea, vomiting, diarrhoea, and abdominal pain. Gentian violet should not be used in the presence of severe heart, kidney, liver or gastrointestinal disease, alcoholism, or coincident infestation with *Ascaris lumbricoides*.

Wright, W. H., and Brady, F. J. (1940) *J. Amer. med. Ass.*, **114**, 861.

Trichuriasis*Treatment*

Iron and ammonium citrate —P. A. Maplestone and A. K. Mukerji, investigating the recent claim of V. Pausa (1937) that large doses of iron and ammonium citrate effectively cure within 10 to 15 days *Trichuris trichiura* infestation, produced evidence which they believed to negative this claim. After 1 week's treatment 5 out of 31 patients treated with an iron and ammonium citrate mixture were negative, of these 2 were not seen again, 2 remained negative until the end of the second week and were not seen again, and 1 became positive by the end of the second week. After 2 weeks' treatment, of the 19 who returned, all but 1 were positive. After 3 weeks' treatment, 8 returned and all were positive. After 5 weeks' treatment all of 5 who returned were positive. In another series of in-patients various salts of iron were tried without results.

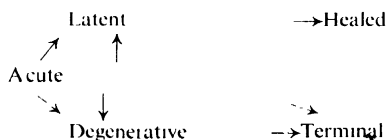
Maplestone, P. A., and Mukerji, A. K. (1939) *Indian med. Gaz.*, **74**, 607
Pausa, V. (1937) *Arch. Med. infant.*, **6**, 469

NEPHRITIS AND NEPHROSIS

See also B. I. M. P., Vol. IX, p. 134, Cumulative Supplement, Key Nos. 1131-1141, and Surveys and Abstracts 1939, p. 443

Classification*Acute Nephritis in Children*

W. W. Payne and R. S. Illingworth consider that the difficult problem of the classification of acute nephritis is unduly complicated. They give a table showing 30 terms in current use to describe forms of nephritis. An analysis is presented of 301 cases of acute nephritis and of 64 other cases seen in subsequent stages among children attending the Great Ormond Street hospital during a number of years. This is a purely clinical investigation, based on blood chemistry, urinary examination, oedema, and blood-pressure, morbid anatomy and histology are excluded. Much detailed argument is devoted to show that acute focal nephritis cannot be diagnosed clinically from acute diffuse nephritis by the absence of nitrogen retention in the focal form and its presence in the diffuse form, the conclusion is reached that acute focal nephritis is not a clinical entity and that no advantage can be gained by such further classification. The adoption of the simple classification proposed by Addis (1925) is advocated (see diagram). Thus acute nephritis may become (a) latent or (b) degenerative, the latent stage is much the commoner,



Addis's Classification

but often escapes recognition, though there is often a gradual rise of blood-pressure, it may pass on into cure or the stages of termination or degeneration. The degenerative stage very rarely passes into the latent stage, but almost invariably into the terminal stage (chronic interstitial nephritis).

Addis, T. (1925) *J. Amer. med. Ass.*, **85**, 163

Payne, W. W., and Illingworth, R. S. (1940) *Quart. J. Med.*, **9**, 37

Morbid Anatomy*Chronic Nephritis*

Associated changes in intestines —J. Felsen regards the intestines as part of a reciprocal excretory system of the body, the other members being the kidneys, lungs, and skin. The common medium of exchange is the circulating blood which, in the case of the intestines, serves as an indirect haematogenous excretory mechanism.

In advanced renal disease associated with uraemic or sub-uraemic states, the urea, chloride, and water contents of the intestinal contents, sweat, and expired air may reach surprisingly high figures, since the intestines, skin, and lungs attempt to take over the functions of the failing kidneys. The associated lesions in the intestinal walls are (i) oedema, (ii) ulceration, and (iii) vascular changes. The oedema may involve the entire wall which becomes thickened to 4 or 5 times the normal. More often, however, the changes are confined to the loose mucosa and submucosa, which often show both diffuse and focal areas of infiltration; sometimes the latter stand out as distinct translucent blebs, varying in size from 1 to 5 cm. with a surface projection of 1 to 3 cm. above the surface. The connective tissue stroma contains much fluid, and the solitary acuminate lymph nodules are greatly enlarged by this accumulation of fluid, and may be completely disintegrated. Ulceration, when present, generally occurs in the distal portion of the ileum and in the colon. The ulcers tend to be discrete and transversely disposed, and are often hidden by folds of mucosa. The latter are sometimes surmounted by punctate haemorrhagic areas of linear necrosis which may represent a somewhat earlier stage than that of frank ulceration. With regard to the lesions in the vessels, these consist essentially of a thickening of the small and large arterial branches with marked diminution in size or occlusion of the vascular lumen. The clinical manifestations are a state of relative anoxaemia with diarrhoea and colic. (Uraemic ulceration was described by Frierichs (1851), Tietz (1859), Dickinson (1867), and Perry and Shaw (1894) - *Ed*.)

Felsen, J. (1940) *Urol. cutan. Rev.*, **44**, 39.

Chemical Pathology

Nephrosis

Hypoaminoacidemia in children with nephrotic crisis. L. F. Farr and D. A. MacFadyen defined the 'nephrotic crisis' as an infection of the blood, sometimes leading to peritonitis, which occurs in nephrotic children because the metabolic changes lower the resistance to bacterial invasion. They found that one of the most striking alterations at this time was in the concentration of the amino-acids in the blood plasma. In nephrosis the plasma amino-acid content is deficient, being between 3 and 4 mg. per 100 c.c.m. instead of 5 mg. or over. During the nephrotic crisis the amino-acid level falls even lower, sometimes as low as 1 mg. per 100 c.c.m., and it may fall very rapidly. The crisis may occur without infection. When the crisis passes, the amino-acid level quickly rises to its former height. In 2 nephrotic children receiving a large amount of protein by mouth, the usual rise in amino-acid level occurred, thus showing that there is no delay in protein absorption and digestion in nephrosis.

Farr, L. F., and MacFadyen, D. A. (1940) *Amer. J. Dis. Child.*, **59**, 782.

Clinical Picture

Nephritis occurring in Syphilis

B. M. Baker discusses the relation of syphilis to nephritis. If nephritis in the course of syphilis is due to that infection, antisyphilitic treatment must be begun without delay. If on the other hand the nephritis is coincident and not related to syphilis, extreme care must be used in giving even the most conservative treatment for syphilis for fear of further damage to the kidneys. Baker found that nephritis was very rarely due to syphilis. The spirochaete has been found in the kidneys in the absence of nephritis. Syphilis probably never produces haemorrhagic and vascular nephritis, but it may play a part in the aetiology of lipoid nephrosis. A true syphilitic nephritis characterized by cells in the interstitial tissue and round the vessels is rare. Baker concluded that syphilitic nephritis should only be diagnosed after an intense search for other causes has proved negative. He reported 2 such cases. Many cases of syphilis associated with nephritis, as in congenital syphilis, are benefited by antisyphilitic treatment, which is therefore not contra-indicated in every case.

Intercapillary Glomerulosclerosis

R. A. Newburger and J. P. Peters report 4 fatal cases of intercapillary glomerulo-

sclerosis. Necropsy showed hyalinization of the glomeruli, which in some cases was complete, but in others confined to the centre of the glomeruli or of individual lobules. The number of capillaries in the affected glomeruli was apparently reduced, and marked arteriosclerosis with fatty degeneration of the arterioles was present. Hyaline material and lipoids appeared beneath the epithelium of the capsule. A summary is given of the clinical features of the condition, based on the above patients and 5 others, of the latter 2 died, but no necropsy was performed. Diabetes mellitus, albuminuria, and hypertension were present in all 9 cases. Retinal changes occurred in 5 of the patients and microcytic anaemia in 4. Oedema occurred in 7 of the 9 cases and was inversely proportional to the level of the serum albumin. Heart-failure when it occurred was usually left-sided, as would be expected in hypertension. The non-protein nitrogen of the blood was raised in 7, none of whom survived more than a year after this had been found. The underlying cause of the condition is extensive arterial and arteriolar degeneration.

Baker, B. M. (1939) *Johns Hopk. Hosp. Bull.*, **65**, 196.

Newburger, R. A., and Peters, J. P. (1939) *Arch. intern. Med.*, **64**, 1252.

Treatment

Nephrosis

Acacia therapy.—D. F. Falkenstein and R. L. Jackson reported the course of nephrosis, and the findings at necropsy in a child of 6 who had been receiving acacia therapy. The authors believed that the ultimate recovery of the nephrotic patient depends on his ability to restore his level of serum protein to normal. Acacia seems to hinder protein synthesis. The interference with serum protein metabolism over a considerable period of time outweighs the transitory benefit from the intravenous use of large doses of acacia. In this case it was found that considerable amounts of acacia remained deposited in the parenchymatous tissues of the body for years after its intravenous administration. During these years the child was unable to increase the serum protein to normal level, even though, during a period of 14 months, he remained essentially free from serious recurrences of the nephrosis.

Concentrated human blood serum.—C. A. Aldrich and H. H. Boyle employed concentrated pooled human serum as a diuretic in 7 cases of pure lipoid nephrosis. All the patients had marked generalized oedema, large amounts of albumin constantly present in the urine, and no red blood-cells in any of the urinary sediment examined. All had normal blood-pressure, normal non-protein nitrogen and blood-urea nitrogen estimations, increased blood cholesterol, and marked decrease in the serum proteins with a reversal of the albumin-globulin ratio. Treatment with serum was begun as soon as feasible in every case. An initial dose of from 25 to 65 c cm. of the 4-times concentrated serum was administered intravenously, and, if diuresis did not follow within 2 days, another injection was given. The maximal number of treatments necessary in any one attack of oedema was 4, and in most cases 1 or 2 were sufficient. Diuresis generally went on to complete elimination of oedema fluid, sometimes to complete recovery from the nephrosis. If the patient showed any evidence of infection, the serum was ineffective.

Glomerulo-Nephritis

Ascorbic acid.—L. Angelini reported on the use of ascorbic acid in glomerulo-nephritis of the haemorrhagic type. The children who usually lose a lot of blood respond best, the administration of ascorbic acid daily is usually sufficient to prevent further permeability of the capillaries and the haemorrhage stops. The author treated 14 patients by this method, with satisfactory results. Diuresis was said to be greatly stimulated, and no further medication necessary.

Effect of Tonsillectomy in Prophylaxis and Cure

R. S. Illingworth studied 365 cases of nephritis in children, 301 of them acute, to see if tonsillectomy is of any value in the prevention or cure of this condition, or if the operation sometimes precipitates it. He found that in the 301 acute cases 20.2 per cent had had their tonsils removed. The incidence of tonsillectomy in London children is only 9 per cent. Tonsillectomy would therefore appear to predispose the child to acute nephritis. In 119 cases tonsillectomy performed in

the acute stage of the disease produced no good result. Of 14 patients suffering from subacute nephritis, 8 had had their tonsils removed during the acute stage. In no case did tonsillectomy prevent the disease from becoming chronic. In 5 per cent of the 301 acute cases tonsillectomy probably caused the disease.

Aldrich, C. A., and Boyle, H. H. (1940) *J. Amer. med. Ass.*, **114**, 1062

Angelini, L. (1939) *Pediatrics*, **47**, 762

Falkenstein, D. F., and Jackson, R. L. (1940) *J. Pediat.*, **18**, 700.

Illingworth, R. S. (1939) *Lancet*, **2**, 1013

NEURALGIA, GLOSSOPHARYNGEAL AND TRIGEMINAL

See also B.E.M.P., Vol. IX, p. 174, and Surveys and Abstracts 1939, p. 445

Trigeminal Neuralgia

Treatment

Vitamin B₁. I. Bakhsh employed vitamin B₁ in 7 cases of trigeminal neuralgia. Of these, 6 responded to treatment, 4 obtaining 100 per cent relief, 1 about 50 per cent, and 1 about 30 per cent. One case did not respond to treatment. The daily dose of vitamin B₁, which was given by intramuscular injection, was about 10 mg. The 4 cases which were completely relieved received 160, 210, 84 and 90 mg. each and in all of them improvement began promptly, and in 2 cases was complete when only 50 mg. had been given, although treatment was continued for a few days longer. The case which obtained 50 per cent relief received a total of 84 mg., and that which obtained 30 per cent relief received 120 mg.

Vitamin B₁ and liver extract. H. Borsook *et al.* treated 58 cases of trigeminal neuralgia, 4 of sphenopalatine neuralgia, and 9 of a typical facial neuralgia, with massive doses of vitamin B₁, and concentrated liver extract. Treatment consisted of, firstly, active therapy, and then a modification of the dietary with some nutritional supplements. The active therapy consisted of intravenous injections of 10 mg. of aneurine hydrochloride daily. About 25 per cent of the patients failed to respond to vitamin B₁ alone, and these were given 0.5 c.c.m. of liver extract, containing 15 U.S.P. anti-anaemia units per c.c.m., intramuscularly, 3 times a week. For those patients who had insufficient relief after several months of treatment with vitamin B₁ and liver, the dose of vitamin B₁ was increased to 100 mg. daily. A high-vitamin low-carbohydrate dietary was given. In most cases this dietary was supplemented by 1 oz. of an aqueous concentration of rice polishings (1,500 I.U. of vitamin B₁) daily, and adequate amounts of other components of the vitamin B₁ complex. The patients were under observation for from 6 to 14 months. Of these, 37 were markedly improved, 15 improved, 3 slightly improved, and 3 unaltered. Of the 52 patients markedly improved and improved, 38 had a remission longer than any spontaneous remission during the 2 years before the beginning of the treatment. Four of the cases of sphenopalatine neuralgia showed no improvement.

Injection of Gasserian ganglion. A. E. Coates described his technique for injecting the Gasserian ganglion in cases of trigeminal neuralgia. He stated that only patients with true paroxysmal *tic douloureux*, ciliary neuralgia, or post-herpetic neuralgia should be subjected to this treatment. Coates found that root-section for post-herpetic neuralgia resulted in complete anaesthesia over the affected area, but the pain persisted. He thought that this was due to pain being associated with the autonomic system, the fibres after leaving the Gasserian ganglion travelling with the cervical sympathetic chain and carotid plexus. X-ray examination of the skull is of no help in locating the ganglion. The patient should lie in bed having received morphine $\frac{1}{2}$ or 1 gr. Lines indicating the temporo-mandibular fossa and the outer canthus of the eye should be drawn on the face with weak solution of iodine. A fine hypodermic needle is inserted 1 inch lateral to and just above the angle of the mouth, and the skin and cheek infiltrated with 2 per cent procaine hydrochloride solution. A 6-inch steel needle of fine bore is then inserted with the finger in the mouth and guided past the pterygoid laminae until it strikes the infratemporal surface of the great wing of the sphenoid. Procaine hydrochloride is next injected into the mandibular fibres. The hilt of the needle is then lifted to approach the foramen

ovale and it is withdrawn slightly. It will then slip into the foramen. A little procaine will numb the pain complained of in front of the ear. The needle is pushed on for $\frac{1}{2}$ inch and then withdrawn to see there is no blood or cerebrospinal fluid in it. Three minims of absolute alcohol is then injected slowly and pressure is required as the ganglion is a solid structure. If the fluid goes in easily the needle is not in the ganglion. This is sufficient for lower ganglion injection, but if the maxillary or ophthalmic areas are affected the needle is turned and pushed on for another $\frac{1}{2}$ inch and another 3 to 5 minims of alcohol injected. The needle is withdrawn and pressure applied at the site of puncture. Eye-drops containing adrenaline are ordered as the eye is reddened, and lateral shields are worn to protect the eyes when the patient is out of doors. If the anaesthesia is not complete 24 hours later a drop or two more alcohol is injected by the same method.

Bakhsh, I. (1939) *Indian med. Gaz.*, **74**, 456

Borsook, H., Kremers, M. Y., and Wiggins, C. G. (1940) *J. Amer. med. Ass.*, **114**, 1421

Coates, A. L. (1939) *Aust. N.Z. J. Surg.*, **9**, 193

NEURITIS

See also B. E. M. P., Vol. IX, p. 182, Cumulative Supplement, Key Nos. 1147-1149; and Surveys and Abstracts 1939, p. 446

Multiple Neuritis

Aetiology

Dietary deficiencies—S. B. Boyd Campbell and R. S. Allison reported 2 cases of toxic polyneuritis with changes in the electrocardiogram. In 1 case, that of a man aged 31, the clinical picture pointed to combined deficiency of both vitamin B₁ and the vitamin B₂ complex. His face, hands, and neck were typical of pellagra (see Fig. 11). The legs were oedematous. There were no definite sensory changes, and he had no pain in the calves or numbness in the hands. Electrocardiograms showed inversion of the T waves in leads II and III, and slight inversion in lead I. Later the T wave was inverted in all leads. There was no evidence of obvious vitamin deficiency in the dietary, apparently there was some temporary interference with absorption. In the second case there was pellagrous dermatitis without polyneuritis or changes in the electrocardiogram. In this case there was a clear history of deficient intake of vitamins, probably aggravated by defective absorption as a result of achlorhydria and diarrhoea. In both cases the condition rapidly improved by the addition to the dietary of the appropriate vitamins, and in the first also by the injection of vitamin B₁.

Treatment

Aneurine hydrochloride—M. G. Vorhaus stated that the administration of adequate amounts of aneurine hydrochloride to cases of polyneuritis is followed by a high incidence of improvement in symptoms.



FIG. 11 Showing swelling and pigmentation of hands. (From *Lancet*, 1940)

This effect generally begins to become apparent within 3 weeks, and by 9 weeks reaches its maximum in most cases. If aneurine is then discontinued, recurrence

of symptoms takes place. At the end of 1 year about one-half of the patients will have had 1 or more recurrences. At the end of 5 years, all, or almost all, of the cases will have had some return of symptoms. The average daily dose of aneurine hydrochloride, given to 520 patients, was 3 to 10 mg (1,000 to 3,000 I U) daily.

Campbell, S. B. B., and Allison, R. S. (1940) *Lancet*, **1**, 738

Vorhaus, M. G. (1939) *Amer. J. med. Sci.*, **198**, 837

NEUROSYPHILIS

See also B.E.M.P., Vol. IX, p. 224, Cumulative Supplement, Key Nos. 1151-1166, Surveys and Abstracts 1939, pp. 154 and 447, and p. 60 of this volume

General Paralysis of the Insane

Treatment

Injection of Rickettsia tsutsugamushi.—R. Kawamura and Ueda used the virus *R. tsutsugamushi orientalis* in the treatment of 20 cases of general paralysis. They injected intramuscularly 0.5 to 1 c.c. of an emulsion of the virus, or 3 to 5 c.c. of the blood of patients infected with the virus, withdrawn during the febrile period. These cases were observed over periods ranging from 1 to 11 months. In 8 cases there was a complete remission of symptoms, in 9 an incomplete remission, in 2 cases no appreciable result, and 1 case died. The authors claimed that the method is as effective as malaria therapy, and that it is free from danger.

Kawamura, R., and Ueda (1940) *Pr. méd.*, **48**, 179

Intracranial Syphilis

'Stationary' General Paralysis of the Insane

A. J. Galbraith records a case of a man, aged 79 years at his death, who for 31 years had been an inmate of Hanwell (now St. Bernard's) Hospital. Between 1908 and 1922 his condition did not seem to alter to any appreciable degree, then signs of further mental deterioration set in, in 1931 advanced dementia was present, and in 1933, when he was 77, general physical deterioration was obvious. In a review of other cases running a prolonged course and even showing spontaneous remissions without treatment, reference is made to Gaupp's patient, who survived for 32 years. In the stationary cases the inflammatory changes in the cerebral cortex have usually been slight. As Galbraith's patient showed a strong positive Wassermann reaction of the cerebrospinal fluid 15 years after the onset and also after death, he can hardly be said to have had a complete remission, and the author suggests that the case would probably be described more accurately as slowly progressive than as stationary.

Galbraith, A. J. (1940) *J. ment. Sci.*, **86**, 112

Gaupp and Alzheimer (1907) *Zbl. Nervenheilk.*, **30**, 696

Spinal Neurosyphilis

Tabes Dorsalis

Associated with syringomyelia.—L. I. Hutton and A. J. Galbraith reported a case in which taboparesis and syringomyelia coexisted. Tabes was the initial disease, becoming apparent first in 1918. Ten years later the symptoms of syringomyelia were observed. It was not until 1937 that the patient showed psychotic manifestations. The authors could not find any published similar case.

Tabetic cord bladder.—J. L. Emmett reviews the present position as regards the 'tabetic cord bladder'. This term has been loosely used and often simply meant an atonic bladder in tabes dorsalis, and might be quite unrelated to neurogenic disease. True urinary incontinence in tabes dorsalis is not common. The symptoms are primarily due to retention and the so-called incontinence is merely overflow from a distended bladder or urgency from urinary infection initiated by the urinary retention. Recent physiology suggests that micturition results from the contractile response to stretching of the muscle fibres in the wall of the bladder, the reflex centre being either in the sacral segment of the spinal cord or, less probably in the author's opinion, local in the ganglion cells of the bladder wall. The higher centres in the cord and brain act only in an inhibitory manner, and until the bladder is

fairly full the impulses that prevent contraction of the bladder arise from a level below the threshold of consciousness. When distension of the bladder becomes greater, the impulses reach the threshold of consciousness and excite the desire to micturate, and the individual will have, if he desires not to micturate, to send more inhibitory impulses to the bladder to prevent it from responding to the reflex desire to contract. If there is a lesion of the sensory roots impairing sensory conduction, the reflex arc would be interfered with and the bladder would become more distended and, as a result, later atonic and flaccid. Recent opinion regards urinary retention as an imbalance between the detrusor urinae muscle and the neck of the bladder; if the detrusor is weak, it would seem reasonable to 'weaken' the neck of the bladder by surgical means so that the detrusor muscle should be able to empty the bladder completely, and this holds good whether the 'atonicity' is neurological or non-neurological in origin. With this object in view transurethral resection has been performed with exceptionally good results at the Mayo Clinic.

Anterior chordotomy for gastric crises—O. R. Hyndman and F. J. Jarvis treated 8 cases of gastric crises in tabes dorsalis by anterior chordotomy. In all 8 cases the treatment was successful. The chordotomy should be done at the second dorsal segment and certainly not lower than the third. It should be bilateral and the spinal thalamic tracts must be completely severed, producing loss of pain sensation to the nipple line. The operation produces transient motor weakness and retention of urine. Loss of sexual function is permanent. There were 2 deaths in this series, 1 from possible cerebral haemorrhage 3 weeks after operation, and 1 from the withdrawal of drugs to which the patient was addicted 2 months after operation.

Acute Syphilitic Transverse Myelitis

S. Berman described a case of acute syphilitic transverse myelitis with paraplegia, which recovered. The pathological process is fundamentally syphilitic, panvasculitis leading ultimately to obliteration by narrowing or thrombosis of spinal blood vessels. The condition occurs most often within the first 3 years after the primary infection. Tests of the blood and spinal fluid generally give positive reactions for syphilis. The protein content of the spinal fluid is elevated, there are an increased cell count and an alteration of the colloidal gold curve which, however, is not characteristic. The prognosis is more favourable in partial than in complete transverse lesions. The results of treatment depend on the extent of injury to the nervous system, the rapidity with which the circulation is re-established and, of primary importance, early well-regulated and sufficient antisymphilitic therapy.

Berman, S. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 1078

Linnett, J. L. (1940) *Proc. Mayo Clin.*, **15**, 91

Hutton, E. L., and Galbraith, A. J. (1940) *Lancet*, **1**, 219

Hyndman, O. R., and Jarvis, F. J. (1940) *Arch. Surg., Chicago*, **40**, 997

Treatment

Side Effects of Arsphenamine Treatment

Nitritoid reactions—F. A. Ellis reported a case of severe nitritoid reaction following the administration of tryparsamide. This was a man of 46 who, after receiving the one hundred and thirteenth of a series of injections of the drug (each of 3 g.), began to experience mild vasomotor reactions, such as flushing of the face and neck. After subsequent injections the symptoms became more severe, and there was a constrictive sensation in the chest, cough, and throbbing sensation in the head. The more severe reactions lasted 30 to 45 minutes. After the last treatment he began to vomit, and experienced severe cramp-like pains in the abdomen, and tightness in the chest.

Ellis, F. A. (1939) *Arch. Derm. Syph., N.Y.*, **40**, 707

OEDEMA

See also B.E.M.P., Vol. IX, p. 268; and Surveys and Abstracts 1939, p. 450.

Aetiology

Hysterical Oedema of Hand and Forearm

C. Williams reported 3 cases of oedema of the forearm and hand in hysterical

subjects, produced by keeping the extremity in an immobile dependent position. In each case the forearm and hand were grossly swollen, and simulated a surgical condition. That the oedema was due to the immobile dependent position in which the arm was held was shown by the prompt recovery which occurred when the limb was fixed in an elevated position.

Williams, C. (1940) *Ann. Surg.*, **111**, 1056.

OEDEMA, HEREDITARY

See also B.E.M.P., Vol IX, p. 282, and Surveys and Abstracts 1939, p. 450

Clinical Picture

Milroy-Nonne Disease

I Herzberg showed a woman, aged 27, with swelling of the arm which began in one finger and spread to the hand and arm. It had begun after several attacks of tonsillitis in 1931; after tonsillectomy in 1938, and lately, the swelling had somewhat diminished. The case was described as 'idiopathic lymphoedema'. Parkes Weber agreed with this diagnosis, but preferred to call the disease the Milroy-Nonne type of oedema of the extremities, which was very seldom limited to the upper extremities.

Lipoedema

I V Allen and I. A. Hines describe a syndrome consisting of fat legs and often orthostatic oedema, chronic, bilateral, made worse by standing, and commonly accompanied by aching. It is often hereditary or familial, but there is never a history of recurrent attacks of acute cellulitis, as in the cases of persistent hereditary oedema described by Hope and French. The patients are usually extremely sensitive to the condition, are always females, in whom the condition may date from girlhood, and they may show neuroses. Generalized obesity may or may not be present, but the legs and buttocks are always extremely fatty, and the adipose tissue shows a peculiar loose texture and the skin and subcutaneous tissues are soft and pliable, but the feet are usually free from oedema. Treatment is usually unsatisfactory, restriction of fluid and the use of diuretics, such as potassium nitrate, are generally without benefit. Heat and gentle massage may relieve distress, and reassurance that the disease is not cardiac, renal, or dangerous to health is important. A table showing the differential diagnosis from Milroy's disease (hereditary oedema) is given.

Allen, E. V., and Hines, E. A., Jnr. (1940) *Proc. Mayo Clin* **15**, 184

Herzberg, I. (1940) *Proc. R. Soc. Med.*, **33**, 330

Hope, W. B., and French, H. (1908) *Quart. J. Med.*, **1**, 312

Weber, F. P. (1940) *Proc. R. Soc. Med.*, **33**, 330.

OESOPHAGUS DISEASES

See also B.L.M.P., Vol IX, p. 287; Cumulative Supplement, Key Nos. 1176-1188; and Surveys and Abstracts 1939, pp. 43 and 450.

Congenital Malformations

Atresia

Surgical treatment.—R Shaw describes the following operation for congenital atresia which is otherwise invariably fatal, usually from aspiration lung lesions. The oesophagus was approached by an extrapleural route and the opening into the trachea closed. The oesophagus was then separated from the trachea and the upper and lower segments of the oesophagus were united by a rubber catheter which passed from the mouth through the oesophagus into the stomach. Although the

immediate result was good, the infant died on the twelfth post-operative day from an extensive bilateral pneumonia

Familial Short Oesophagus

R. B. Myles describes radiological appearances which are not characteristic of para-oesophageal hernia, but of congenitally short oesophagus with partial thoracic stomach. This condition was suggested in a mother and daughter. Clinically there are attacks of pain not explained by other causes, such as gall-bladder disease, which is least when the patient is in the erect position, worse in bed, and worst on stooping down. Some relief follows elevation of the head of the bed. The condition should be distinguished from congenital hernia of the diaphragm described by G. Schreiber.

Myles, R. B. (1939) *Brit. J. Radiol.*, **12**, 645

Schreiber, G. (1922) *Bull. Soc. Pédiat. Paris*, **20**, 189

Shaw, R. (1939) *J. thorac. Surg.*, **9**, 213

Oesophageal Varices

Treatment

Injection of sodium morrhuate—H. J. Moersch records the injection of varicose veins in the lower third of the oesophagus, so large as almost to occlude the lumen. Four injections of 0.5 c.c. of a solution of 2.5 per cent of sodium morrhuate at 4 days' intervals were given. A man, aged 30, had since 1928 had several severe attacks of gastro-intestinal haemorrhage, and his spleen, 9 times the normal size, had been removed in 1929, but bleeding recurred. X-rays showed the presence of oesophageal varices, which appeared through the oesophagoscope to be large, bluish, nodular, soft compressible projections. It was rather surprising that the injections did not cause bleeding. A diagnosis of hepatic cirrhosis was made.

Moersch, H. J. (1940) *Proc. Mayo Clin.*, **15**, 177

OVARY DISEASES

See also B. I. M. P. Vol. IX, p. 318, and Surveys and Abstracts 1939, p. 451

Tumours

Dysgerminoma

M. B. Dockerty summarized 9 cases of dysgerminoma of the ovary. Seven of the cases were unilateral, 5 were associated with uterine hyperplasia, and one was accompanied by pregnancy. All the tumours were malignant but recurrences occurred in only two cases. Three of the patients died after operation. Dockerty stated that dysgerminomas are often associated with hypoplasia of the genital organs and occur in a condition of pseudohermaphroditism. They occur as seminomas in the male and are then even more malignant, and usually appear after 20 years of age. Dysgerminomas in the female usually appear before twenty. Since the tumour produces no hormone it does not give rise to sexual or menstrual disturbances. It is a solid smooth tumour of brain-like consistency and containing a good deal of necrosis and haemorrhage. Microscopically the tumour contains large round cells with a small amount of cytoplasm. There are many mitotic figures and a loose stroma infiltrated with lymphocytes and an occasional large foreign-body giant cell.

Theca and Granulosa-Celled Tumours

H. F. Traut and A. A. Marchetti report an investigation of 54 ovarian theca-granulosa-celled tumours. In most cases staining by Foot's silver method renders it possible to differentiate theca from granulosa cells. The so-called granulosa-celled tumours contain varying numbers of theca-cell elements, so that pure granulosa-celled tumours are rare. Several growths in this series contained equal proportions of the two cell types. Most of the so-called theca-celled tumours also

contained granulosa elements in considerable proportions. In the series were one pure granulosa-celled tumour, and four pure theca-celled tumours.

Dockerty, M. B. (1939) *Proc. Mayo Clin.*, **14**, 545.

Traut, H. F., and Marchetti, A. A. (1940) *Surg. Gynec. Obstet.*, **70**, 632.

Ovarian Hypernephroma

I. W. van Kirk and L. A. Edwards report a case of a solid and pseudo-cystic tumour of the left ovary, which weighed 6 lb., in a woman, aged 42 years, who had had increased menstruation. The authors review the literature on the debatable point whether these tumours are derived from accessory adrenals embedded in the ovary or are lutein-celled growths. Peham (1899) first used the title ovarian hypernephroma, and since then this origin has been accepted by about 27 writers. This was opposed by Glynn (1912) and by Turnbull (1920) in Great Britain and their view has been widely accepted. Van Kirk and Edwards, however, consider that the histological appearances and the glycogen content of the tumour in their case suggest a hypernephroma rather than a lutein-celled growth. Five at least of the ovarian hypernephromas they collected were malignant.

Glynn, F. F. (1912) *Quart. J. Med.*, **5**, 157.

Peham, H. (1899) *Msch. Geburtsh. Gynak.*, **10**, 685.

Turnbull, H. M. (1920) see Gordon, A. K. *Brit. med. J.*, **1**, 133.

Van Kirk, F. W., and Edwards, L. A. (1939) *Amer. J. Cancer*, **37**, 209.

OZAENA

See also B. E. M. P., Vol. IX, p. 354, and Surveys and Abstracts 1939, pp. 90 and 453.

Treatment

Oestrogenic Substance

W. W. Eagle *et al.* treated patients suffering from atrophic rhinitis with oestrogenic substances. The nose was irrigated twice daily with physiological saline, or 1 in 10,000 solution of potassium permanganate, and 10 minutes later the irrigation was repeated to remove the crusts. Then 0.5 c.cm. of oestrogenic substance, equivalent to 500 I.U., was sprayed into the nose twice daily. Twenty-one of the patients were clinically improved. In 14 of the cases the crusts were either completely removed or diminished. The characteristic odour associated with the disease was prevented and the nasal mucosa became pink and smoother. In these 14 cases biopsy of the nasal mucous membrane was done. There were no marked changes, but the mucus of the glands was slightly increased and the connective tissue was somewhat looser. This last change may have been due to oedema.

Eagle, W. W., Baker, R. D., and Hamblen, E. C. (1939) *Arch. Otolaryng., Chicago*, **30**, 319.

PAIN

See also B. E. M. P., Vol. IX, p. 359; and Surveys and Abstracts 1939, pp. 19 and 454.

Treatment

Cobra-Venom for Intractable Pain

R. N. Rutherford investigated the use of cobra-venom in the relief of intractable pain. He reported 17 cases of such conditions as carcinoma of the cervix, interstitial cystitis, carcinoma of bladder, and carcinoma of breast which were given from 1 c.cm. (5 mouse units) every 3 days to 1 c.cm. three times a day of cobra-venom. Of these patients 46 per cent were completely relieved of pain, and 88 per cent were relieved of half or more of their pain. In the cases which were only partially relieved the addition of a mild non-habit-forming analgesic was sufficient to completely relieve them. The general health of those benefited improved, and many

of them were able to return to work. The venom was given intramuscularly and the active principle it contains appeared to be a 'neurotoxin'

Rutherford, R. N. (1939) *New Engl. J. Med.*, **221**, 408

PALATE, CLEFT, AND HARE-LIP

See also B. L. M. P., Vol. IX, p. 373, and Surveys and Abstracts 1939, p. 454

Hare-Lip

Treatment

New Cupid's-bow operation—E. A. Hardy describes a new Cupid's-bow operation for hare-lip with some advantages. Advancement of the lip and base of the nose is made by the recognized incision along the line of reflexion of the mucosa in the labial sulcus behind the columella and alae. The tissues are thus freed from their bony attachment but, before the impression of the raw area is taken, another incision is made at the junction between the skin and the vermillion border. The mucosa is dissected from behind the whole length of the lip, and lowered to the desired position. The vermillion border now consists of only two thicknesses of thin membrane, between which more substance must be incorporated. The mass of orbicularis oris muscle bunched up in the centre of the lip is divided horizontally from behind, and the lower portion pulled down between the two layers to form the body of the new vermillion border. The Stent mould over which the graft is stretched creeps into this division between the muscle fibres and holds them in place. The operation is completed with gossamer silk-worm gut sutures at the junction of the skin and mucosa. The lowering of the lining to the lip increases the raw area above, which requires a slightly larger Thiersch graft. The lip is held in this position until the graft is fully established, then the middle is allowed to recede to produce the desired concavity.

Hardy, E. A. (1940) *Lancet*, **1**, 361

PANCREAS, DISEASES

See also B. L. M. P., Vol. IX, p. 386, and Surveys and Abstracts 1939, p. 455

Physiology

Lipocae

L. R. Dragstedt stated that, although the beta cells of the islets of Langerhans are known to produce insulin, the function of the alpha cells is unknown. It is, however, impossible to keep depancreatized animals alive on insulin alone. At necropsy these animals show extensive degeneration and fatty infiltration of the liver, and in one experimental animal there was arteriosclerosis of the aorta. Pancreatic extract by mouth corrects this deficiency in dogs. It was thought that the leucithin and choline contained in these extracts exerted a beneficial effect, but an extract has been prepared which does not contain these compounds and it is just as effective. Fatty infiltration of the liver may be induced by inadequate insulin therapy leading to lipid deposits. This is corrected by giving the patient more insulin. It may also be due to a low concentration of blood lipoids and impaired liver function. This form is unaffected by insulin but is cured by giving lipocae, the active principle in the alpha cells. Arteriosclerosis also occurs commonly in diabetes mellitus and is probably due to lack of lipocae, as suggested by the results of animal experiment.

Dragstedt, L. R. (1940) *J. Amer. med. Ass.*, **114**, 29.

Developmental Abnormalities

Annular Pancreas

G. J. Cunningham reported a case of annular pancreas, a rare condition. Hypotheses of its causation include a simple hypertrophy of the pancreas, and a

developmental error of the pancreatic anlagen. The case reported was that of a man of 65 years who died of uraemia. The condition, which had given rise to no symptoms, was found at necropsy. A band of pancreatic tissue was found surrounding the second part of the duodenum. The origin of the abnormality was shown to be from the ventral bud, thus confirming the more usual embryological hypothesis of origin.

Cunningham, G. J. (1940) *Brit. J. Surg.*, **27**, 678.

Acute Inflammatory Conditions

Acute Interstitial Pancreatitis and Acute Pancreatic Necrosis

Conservative treatment—M. A. Casberg reported 5 cases of acute interstitial pancreatitis and 5 of acute pancreatic necrosis, all of which were treated conservatively; all the patients in the first group recovered, and all in the second group died. According to Casberg all patients with acute pancreatic necrosis should be operated on after suitable pre-operative treatment. The lesser sac should be drained to allow the trypsin to be evacuated without acting on the pancreas and surrounding tissues. In interstitial pancreatitis the symptoms are transient and the patients soon recover. The two conditions can be differentiated because acute interstitial pancreatitis is not fulminating and does not produce shock and circulatory collapse. In both there is epigastric pain, and both conditions can be diagnosed early by the rise in blood amylase. Some patients are jaundiced. The condition is thought to be due to regurgitation of bile into the pancreatic system, which may be followed by necrosis and infection. Death is due to toxæmia from absorption of the necrotic glandular elements.

Acute Pancreatitis

Surgical treatment—J. J. Morton and S. Widger stated that, in cases of acute pancreatitis, time should be taken to get the patient into the best possible condition before operation. Shock should be adequately treated and the fluid balance restored. In very ill patients the simplest surgical treatment should be undertaken. If jaundice is present, drainage of the gall-bladder or common duct may be employed. The pancreas should be disturbed as little as possible, because it cannot be drained by splitting the capsule, as was formerly advocated.

Casberg, M. A. (1939) *Arch. Surg., Chicago*, **39**, 247.

Morton, J. J., and Widger, S. (1940) *Ann. Surg.*, **111**, 851.

Tuberculosis

R. R. Little reports a case of tuberculosis of the pancreas, an exceedingly rare condition. This case was unique in that it was characterized by a disturbance of pancreatic function. The clinical picture was that of an advanced pulmonary tuberculosis complicated by diabetes mellitus. Large and increasing doses of insulin were necessary to maintain the blood-sugar near normal limits. Persistent and distressing epigastric pain was an important feature. The patient steadily went downhill. At necropsy there was found caseous and proliferative tuberculosis of the lungs with bilateral cavitation. The head of the pancreas was reduced to a mass of apparently normal pancreatic tissue about 5 cm. in greatest width and 3 cm. in thickness. The remainder of the pancreas was for the most part replaced by firm fibrous tissue, containing at the splenic end a smooth-walled cyst, 2 cm. in diameter, filled with creamy, purulent fluid in which acid-fast organisms were seen in a direct smear. The pancreatic duct was patent, and the bile duct was not involved. Microscopically there were occasional tubercles containing typical giant cells. Tuberculosis of the pancreas can be diagnosed with certainty only post-mortem, but it should be suspected in the presence of persistent and constant epigastric pain in a tuberculous patient.

Little, R. R. (1940) *New Engl. J. Med.*, **222**, 135.

Tumours

Diagnosis

J. E. Dunphy considers that, as surgery now offers hope to patients with cancer of the pancreas, it is imperative to recognize its earliest manifestations. Before

the onset of jaundice accurate diagnosis is extremely difficult. Important symptoms are persistent inexplicable abdominal pain, radiating to the back, worse at night or when the patient is lying down, and rapid loss of weight. Unexplained, intractable diarrhoea, persistent nausea unrelated to meals, or a peculiarly obstinate epigastric distress though uncommon may, however, suggest the diagnosis. X-ray examination may contribute positive as well as negative evidence.

Carcinoma

M. Loeper *et al* reported a case of carcinoma of the pancreas which had invaded all the neighbouring organs and which presented 3 interesting features, as follows: (1) Disseminated nodules were found in the lungs; these cancerous metastases were larger, less transparent, and less white than those of tuberculous granulomas, and were surrounded by a red areola. (2) Cancerous cells were present in the bone marrow. (3) Erythroblastosis, or the appearance in the blood of a number of nucleated elements in various stages of development, from the pro-erythroblastic to the normoblastic stage. The authors advance three hypotheses to explain cancerous erythroblastosis: (1) impoverishment of the terrain due to the cancerous process robbing the cells of nourishing substances and so preventing them from maturing, (2) the destruction of the cancerous cells liberates lysine, histidine, and arginine, which may over-stimulate the haematopoietic organs to an activity which remains partly abortive, (3) the production of toxic substances, such as lactic acid, which probably stimulate erythropoiesis.

Dunphy, J. L. (1940) *Amer. J. digest. Dis.*, **7**, 69.

Loeper, M., Mallarmé, J., and Brault, A. (1939) *Pr. méd.*, **47**, 1205.

PARATHYROID GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 424, and Surveys and Abstracts 1939, p. 459.

Hypoparathyroidism

Clinical Types

Symmetrical cerebral calcification.—L. McK. Eaton and S. F. Haines stated that symmetrical cerebral calcification, particularly of the basal ganglia, is often associated with parathyroid insufficiency. The condition is rare. They reported three cases characterized by convulsions, mental deterioration, a low blood-calcium, and cerebral calcification in the region of the basal ganglia which was well demonstrated by X-rays. Two of the patients had diminished vision and one, a woman of 28 years, had bilateral immature cataracts. The patients were treated with cod-liver oil and calcium lactate in large doses. One patient did not return and was not followed up, but in the other two physical improvement was great, the convulsions ceasing, and mentally the patients improved considerably. The authors concluded that in all cases of parathyroid insufficiency the skull should be X-rayed, and in all cases in which symmetrical cerebral calcification is found, the serum calcium should be determined.

Treatment

Dihydrotachysterol.—A. Bloxson also successfully treated with dihydrotachysterol an infant of several weeks of age who was believed to have parathyroid tetany. The blood calcium before treatment was 5.4 mg. per 100 c.cm., and the phosphorus 6.2 mg. Even though calciferol and calcium gluconate were given, the calcium content fell further, and no improvement in the symptoms of tetany occurred. No calcium was found in the urine. Dihydrotachysterol, 5 drops 3 times a day, was given, after 3 days this dosage was increased to 10 drops, 3 times a day, then after another 5 days the dosage was increased to 15 drops, 3 times a day. The child showed signs of improvement, and the blood calcium rose to 11.4 mg., and the phosphorus fell to 4.5 mg. per 100 c.cm. The urine showed a precipitate of calcium with Sulkowitch's test which is carried out by adding equal amounts of Sulkowitch's reagent (2.5 g. of oxalic acid, 2.5 mg. of ammonium oxalate, and 5 c.cm. of glacial acetic acid are dissolved in distilled water and made up to a volume of 150 c.cm.) to the urine. If the calcium content is satisfactory a precipitate of the calcium present comes down as a fine white cloud of calcium oxalate. The dosage of dihydro-

tachysterol was gradually decreased to 1 drop, 3 times a day and finally discontinued. Calcium and calciferol were continued, and the child had progressed well.

J. E. Berk reported a case of idiopathic hypocalcaemia, probably of parathyroid origin, which was successfully treated with dihydrotachysterol (A.T.10). The patient, a woman of 54 years, suffered from fatigue, cramps, and attacks of tetany. Her serum calcium was low and the phosphorus high. X-ray examination showed the bones to be unaffected. The urinary calcium excretion was very low. She was given a high calcium-low phosphorus diet, calcium lactate by mouth and vitamin D. A.T.10 was then given and it was found that 0.75 c.c.m. daily, in addition to the other measures, kept her blood calcium at normal level and kept her free from symptoms. The dose necessary varies in different individuals, and Berk warned against too large a dose as the drug is cumulative and hypercalcaemia may be produced. The serum calcium must be determined frequently during treatment. The drug acts for some days after its administration. It has no effect on cataractous changes in the eye once they have formed in hypoparathyroidism.

I. Rose and F. W. Sunderman treated 5 patients with parathyroid deficiency following thyroidectomy with a 0.5 per cent solution of dihydrotachysterol in sesame oil. Of this solution they were given 10 c.c.m. daily for three days, followed by maintenance doses of 2 c.c.m. daily until the serum calcium and phosphorus had returned to normal and all symptoms had stopped. Then a few doses of 2 c.c.m. of the solution were given each week and in some cases calcium lactate was also added. In all patients the treatment was successful, but it was found that excessive doses could produce hypercalcaemia and toxic symptoms. Analysis showed that the urinary excretion of calcium is increased at the expense of the faecal.

Post-Operative Tetany

Parathormone-shock treatment — L. J. Adams records the dramatically beneficial effect of dihydrotachysterol (A.T.10) on a severe case of post-operative tetany, and summarized the reports on this form of treatment since it was introduced by Holtz in 1933. It exerts a specific and profound influence on the concentration of calcium in the blood, namely a rise in the blood content which is more prolonged than that of parathyroid extract, a single dose lasting many days. In this case dihydrotachysterol was given by the mouth, at first 1 c.c.m. and then 2 c.c.m. daily for a time, subsequently a maintenance dose of 1 c.c.m. twice a week kept the patient, who had undergone subtotal thyroidectomy for toxic goitre, in fair health. At least 2 parathyroids had been removed. Under the title 'parathormone shock-treatment in post-operative tetany' J. H. Mullin and F. Elliott report a very complicated case of a woman, now aged 47, who had been under observation for 40 years and may have had, with other members of her family, a congenital deficiency of calcium. In 1924 she had tetany after removal of a goitre, but gradually recovered, in 1932 the tetany recurred, and the shock treatment, coma being produced, was carried out, and then there was improvement. Subsequently, in 1938, she was given dihydrotachysterol instead of parathormone, but the shock treatment was not repeated.

Adams, I. J. (1940) *Canad. med. Ass. J.*, **42**, 373.

Berk, J. E. (1939) *Endocrinology*, **25**, 984.

Bloxom, A. (1940) *J. Pediat.*, **16**, 344.

Faton, I. M., and Haines, S. F. (1939) *J. Amer. med. Ass.*, **113**, 749.

Holtz, F. (1933) *Arch. klin. Chir.*, **177**, 32.

Mullin, J. H., and Elliott, F. (1940) *Canad. med. Ass. J.*, **42**, 345.

Rose, E., and Sunderman, F. W. (1939) *Arch. intern. Med.*, **64**, 217.

Hyperparathyroidism

Clinical Features

In children — W. E. Anspach and W. M. Clifton stated that hyperparathyroidism resulted in muscular weakness, polyuria, pains in the bones and skeletal changes, and renal colic caused by stones, diarrhoea, and loss of appetite might also be present. The serum calcium and phosphorus are decreased and the urinary excretion of calcium increased. They reviewed the literature of the condition and reported 2 cases occurring in children, girls aged 11 and 4 years. In the first case symptoms

began when the child was 9 years old and were the same as those found in adults. She had generalized osteoporosis and metastatic calcification in a tendon round the right knee joint and in the right acromial bursa. A parathyroid adenoma was present and its removal cured the condition. In the second case symptoms were first noted at the age of 3 months and the case was thought to be one of primary hyperparathyroidism. There was polyuria, weakness and bony changes. Blindness developed, probably due to increased intracranial pressure caused by changes in the bones of the skull. The bony changes resembled those found in renal rickets. Irradiation of the neck with X-rays produced an improvement. The bones recalcified and the muscular weakness and polyuria were relieved.

Anspach, W. L., and Clifton, W. M. (1939) *Amer. J. Dis. Child.*, **58**, 540

PAROTID GLAND DISEASES

See also B I. M. P., Vol. IX, p. 449, Cumulative Supplement, Key Nos. 1217, 1226, and Surveys and Abstracts 1939, p. 461

The Premenstrual Salivary Syndrome

W. Racine describes 4 cases of women with similar symptoms. The first patient who had a year previously undergone a partial ovariectomy suffered 4 to 5 days before every period from painless swelling of the parotid gland, and swelling of the breasts. The second patient had also had swelling of the right parotid 4 to 5 days before the period since she had an unilateral ovariectomy 7 years previously. For the previous 3 months the submaxillary gland had also swelled shortly before the menstruation period, there was also swelling of the breasts. The third patient had been sterilized 15 years before, and for 5 months had had swelling of one parotid and of the submaxillary glands and breasts. The fourth patient had had a curettage since when the period had disappeared, every month swelling of the submaxillaries and the breast occurred and lasted for 4 to 5 days. A sialogram showed dilatation of the excretory channels of the parotid during the period of swelling. Microscopic examination of the submaxillary showed a similar process. After discussing some differential diagnostic possibilities such as disease, lithiasis, tumour, tuberculosis, and infection the author discusses the aetiology of this specific syndrome. The salivary glands are connected with the nasal secretory glands and, in the author's cases, appeared to be influenced by the ovaries. As the salivary syndrome happens during the luteinization period of the menstrual cycle, it is believed that it indicates a state of hypoluteinism. The swelling of the breasts indicates that there is hyperfolliculism. Injections of proluton (corpus luteum hormone) caused the swellings to disappear which appears to prove that the author's aetiological theory is correct.

Racine, W. (1939) *Schweiz. med. Wschr.*, **69**, 1204.

Acute Secondary Parotitis

Treatment

Lugol's solution—D. J. Leithauser and M. O. Cantor employed massive doses of Lugol's solution in 13 cases of acute secondary parotitis with satisfactory results. The average daily dose was 160 minims, 20 minims every 3 hours day and night. In fulminating cases, an additional one or two fl. drachms were given intravenously or subcutaneously, one fl. drachm in 1,000 c.cm. of saline or glucose. This dosage was continued until the inflamed gland showed definite signs of improvement, then the dosage was gradually decreased, and discontinued when the active process had subsided. If an abscess formed the gland was not incised, but aspirated daily through a large-calibre needle. The average time of recovery was 5½ days. Two cases suppurated. There were no deaths.

Leithauser, D. J., and Cantor, M. O. (1940) *Ann. Surg.*, **111**, 650

Acute Suppurative Parotitis

Treatment

X-ray therapy—A. J. C. Latchmore *et al.* employed deep X-ray therapy in 11 cases of suppurative parotitis with impressive results. Of 7 cases given immediate treat-

ment, a complete resolution occurred in 5, resolution after incision of a local abscess occurred in 1, and in another resolution was in progress at the time of the patient's death from other causes. In 2 cases treated after the parotitis had been apparent for 2 days, one resolved completely, in the other local abscess formation occurred; in 2 cases treated later in the course of the infection, X-rays had little apparent effect. The technique was as follows: A small dose, generally 100 *r* daily or 200 *r* on alternate days, was given to a skin field sufficient to cover the swelling. The total dose was 500 to 600 *r* to the skin, equivalent to about 300 *r* to the deepest part of the parotid gland. In most cases the treatment was given at 200 kv., 1 mm. copper filter, and focal skin distance 23 cm. The important point in treatment is that it should be applied immediately, if possible within a few hours of the appearance of the parotid swelling.

Latchmore, A. J. C., La Touche, A. A. D., and Shucksmith, H. S.
(1940) *Lancet*, **1**, 497

PELLAGRA

See also B F M P., Vol. IX, p. 468, Cumulative Supplement, Key No. 1228, and Surveys and Abstracts 1939, pp. 149 and 461

Aetiology

H. S. Stannus reviews the present position about the aetiology and treatment of pellagra. In 1936 he supported the hypothesis that there was a synthesis of a pellagra-preventing factor in the stomach, analogous to Castle's factor in connexion with Addisonian anaemia, and now argues that in pellagra there is a faulty production of coenzyme (codehydrogenase) which is normally present in the body and catalyses the oxidation of certain metabolites by activating the hydrogen of the substrate. The blood content of coenzyme is low in pellagra, and can be raised by the administration of nicotinic acid (Vilter *et al.*) which is a component of the coenzymes I and II. The coenzyme factor is, like coenzyme, found in all animal tissues and in yeast, and is regarded as the normal physiological agent for the oxidation of coenzymes I and II. The therapeutic results obtained from the administration of nicotinic acid and of riboflavin are conflicting, Spies *et al.* reported cases which responded to nicotinic acid but not to riboflavin and vice versa. With regard to the lesions at the angles of the mouth, palpebral fissures, lips with the anterior nares, prepuce, anus, vulva, and scrotum, the author has found that the skin in these areas has a very fine texture and histologically presents peculiarities which, combined with liability to trauma and being often moist and warm, render them liable to be affected.

Spies, T. D., Bean, W. B., and Ashe, I. (1939) *Ann. intern. Med.*, **12**, 1830.

Stannus, H. S. (1936) *Trop. Dis. Bull.*, **33**, 729.

— (1940) *Lancet*, **1**, 352.

Vilter, R. W., Vilter, S. P., and Spies, I. D. (1939) *Sth. med. J.*, **32**, 619.

Clinical Picture

Cheilitis

Sebrell and Butler (1938) described 'cheilitis' as being a characteristic feature of riboflavin deficiency. The lesion of cheilitis consists of redness, desquamation, and finally ulceration of the lips at the mucocutaneous junction. Fissures at the corners of the mouth may also develop. The lesion appears in pellagra, and may do so before any of the signs of pellagra are present. Likewise nicotinic acid may cure the neurological manifestations of pellagra and leave the cheilitis unaffected. R. W. Vilter *et al.* then found that the lesions healed if large doses of riboflavin were given. V. P. Sydenstricker *et al.* reported 5 cases showing the typical lesion of riboflavin deficiency, and a sixth case suffering from an atypical dermatitis of the hands. Five of these patients suffered from pellagra. Two of them presented cheilitis, conjunctivitis, and dermatitis together, all of which were cured by large doses of riboflavin. The lesions in the other patients were also cured by the drug and a

suitable diet. Riboflavin was more efficient when given parenterally in doses up to 50 mg daily subcutaneously or 25 mg intravenously, than by mouth; the dosage by mouth was 10 to 20 mg daily.

Sebrell, W. H., and Butler, R. F. (1938) *Publ. Hlth. Rep., Wash.*, **53**, 2282.

Sydenstricker, V. P., Geeslin, L. E., Templeton, C. M., and Weaver, J. W. (1939) *J. Amer. med. Ass.*, **113**, 1697.

Vilter, R. W., Vilter, S. P., and Spies, T. D. (1939) *J. Amer. med. Ass.*, **112**, 420.

Treatment

Quinolinic Acid

R. W. Vilter and T. D. Spies studied the response of seven patients suffering from pellagra to quinolinic acid. Six patients were given 1 g. by mouth in divided doses over a period of 5 hours. The response to treatment was immediate. The stomatitis faded within 6 hours and the tongue and mucous membranes were of normal colour within 24 hours. All the patients felt better and stronger for the treatment. Mental symptoms, confusion, apprehension, and instability occurred in one patient but he recovered within 24 hours. One severely ill patient was given 1 g. every day for 3 days. Within 48 hours the colour of the tongue was normal, the Vincent's angina had disappeared, and dermatitis of the feet had begun to heal. In pellagrins the blood concentration of coenzymes I and II is decreased. In these 7 cases it was normal within 24 hours of treatment.

Vilter, R. W., and Spies, T. D. (1939) *Lancet*, **2**, 423.

PEMPHIGUS AND PEMPHIGOIDS

See also B. L. M. P., Vol. IX, p. 482, Cumulative Supplement, Key Nos. 1229-1233, and Surveys and Abstracts 1939, p. 463.

Pemphigus Acutus

Aetiology

From a study of the aetiology of pemphigus, I. Markoff and H. Knauer found a close connexion with exfoliative dermatitis. By means of cultures on the chorio-allantoic membrane they obtained bodies, which resembled the Paschen bodies of smallpox. This led them to believe that pemphigus may be caused by a virus, though it was as yet impossible to isolate the organism.

Markoff, I., and Knauer, H. (1939) *Arch. Kinderheilk.*, **118**, 39.

Pemphigus Neonatorum

Treatment

Sulphapyridine.—A. G. Troup and R. M. White reported a case of pemphigus neonatorum which was successfully treated with sulphapyridine. The infant's skin had begun to peel on the hands and feet on the first day after birth. This peeling gradually spread all over the body until the 12th day of life when blisters appeared. These also spread over the trunk and limbs and became dirty and oozed pus. The child was breast-fed and had green loose stools. There was no sign of infection in the mother. The patient's general condition was very grave on admission to hospital. The infected areas were cleaned with flavine and dressed with a 4 per cent solution of silver nitrate in spirit followed by a 1 per cent solution of gentian violet in spirit. This dressing was repeated twice a day. Sulphapyridine, 0.125 g., was given 6-hourly. Starch poultices followed by Lassar's paste were put on the scalp and face. Some fresh bullae appeared on the feet, but they were the only fresh lesions to appear during the treatment. Material taken from the bullae was cultured, but haemolytic streptococci could not be found. After 3 days' treatment the lesion had so improved that the local applications of silver nitrate and gentian violet were stopped. After 5 days the sulphapyridine was discontinued and a few days later Lassar's paste was stopped. After 20 days the patient was discharged from hospital completely cured.

Troup, A. G., and White, R. M. (1939) *Lancet*, **2**, 1367.

PENIS AND SCROTUM DISEASES

See also B.E. M.P., Vol. IX, p. 498, and Surveys and Abstracts 1939, p. 465

Plastic Induration of Penis

I. P. Johnson discussing 'plastic induration of the penis' regards the condition as being possibly traumatic in origin and progressively aggravated by coitus. The author has seen 12 cases in 10 years and finds that two-thirds of those reported are in the fifth and sixth decades of life. The disease affects the dorsum or sheath of the corpora cavernosa or the septum between the corpora, and appears as a thickened elongated node in the middle of the shaft of the penis. Histologically the swelling represents bundles of collagen fibres interspersed with spindle-shaped nucleated cells or fibroblasts, the whole structure being keloid in type. The most constant symptom is deformity of the penis, typically characterized by a dorsal curvature and frequently by a bending to one side or the other. Pain, usually present only on erection, ultimately renders coitus impossible. Although recurrences are frequent, surgical removal of the mass of fibrous tissue through a longitudinal incision, which avoids the median dorsal veins, gives the best results. Haemorrhage is avoided by a tourniquet being placed round the base of the penis prior to operation.

Johnson, F. P. (1940) *Northw. Med., Seattle*, **39**, 22

PEPTIC' ULCER

See also B.E. M.P., Vol. IX, p. 504, Cumulative Supplement, Key Nos. 1236 and 1237, Surveys and Abstracts 1939, pp. 46, 167, and 466, and pp. 5, 12, and 25 of this volume

Aetiology

D. Jennings, in a review of the age-incidence and sex-distribution of perforated peptic ulcer during the last 150 years, showed that, between 1850 and 1900, of every 6 free perforations into the peritoneal cavity, 3 occurred in young women under 25, one in an elderly woman, one in an elderly man, and one in a young man. Since 1920, of every 10 perforations, one has affected an elderly woman, and 9 men mostly of middle age or younger. Perforations in young women formed a sharply defined group which increased rapidly at the beginning of the 19th century and died out completely and suddenly at the beginning of the 20th. This type of ulcer must therefore have been due to something in the environment, or in the mode of life. Perforated pyloric ulcers in men can also be shown statistically to fall into at least two independent groups. One group is closely associated with, and inseparable from, perforations of the lesser curvature; the other tends to affect younger men and has recently undergone a great increase in north-west Europe. Something in the mode of life appears to be responsible also for this type of perforation. It is argued that perforated peptic ulcers should be notified, the information thus obtained would be of service in elucidating the mechanism and in assisting prevention of the condition.

Effect of Gastric Acids

W. I. Palmer and P. B. Nutter investigated the question whether or not peptic ulcer occurs in the complete absence of acid gastric juice. They concluded that small acute and subacute gastric ulcers might occur in achlorhydria, as proved by the histamine test, but that large chronic ulcers occur only in the presence of acid gastric juice. The latter therefore plays an essential part in the origin and course of chronic gastric ulcer.

Relation of Blood Carbon Dioxide and Dehydration to Gastric Acidity

I. W. Taylor and A. C. Michael report an investigation by means of the Pavlov pouch in healthy dogs to find a correlation between the plasma CO_2 and the gastric acidity, but without success. Depression of the plasma CO_2 to 26 volumes per cent by feeding with ammonium chloride did not diminish the free acidity of Pavlov pouches. With the administration of this salt there was a great increase in the pouch secretion which was attributed to a coincidental water intake from thirst produced

by salt ingestion. The importance of evaluating the total amount of effective free acid is emphasized rather than the estimation of free acid 'clinical units' only. Dehydration was quite effective in reducing the amount of pouch secretion, but caused only a little change in the free acid. Dogs can be maintained for days on such a dehydration regime without apparent distress or harm.

Jennings, D. (1940) *Lancet*, **1**, 395 and 444.

Palmer, W. L., and Nutter, P. B. (1940) *Arch. intern. Med.*, **65**, 499.

Taylor, F. W., and Michael, A. C. (1940) *Amer. J. digest Dis.*, **7**, 67.

Pathology and Morbid Anatomy

Site of Chronic Ulcers

From analysis of 272 (males 220, females 52) consecutive operations for chronic benign gastric ulcer at the Mayo Clinic, O. T. Clagett obtained the following figures about the site of the ulcer: 98 patients, or 36 per cent, had such ulcers on the lesser curvature at the angle of the stomach; 84 patients, or 31 per cent, on the lesser curvature above the angle; 43 patients, or 16 per cent, on the lesser curvature between the angle of the stomach and the pylorus; 41 patients, or 15 per cent, on the posterior wall of the stomach near the angle; 4 patients had ulcers on the greater curvature, and 2 patients on the anterior wall of the stomach.

Clagett, O. T. (1940) *Proc. Mayo Clin.*, **15**, 337.

Clinical Picture

Pernicious Haemorrhage

In a discussion of the surgical treatment of gastro-duodenal haemorrhage, J. B. Harman isolates a group of cases which differ so much in pathology, course, and response to treatment from other forms (acute ulcer, gastrostaxis, and chronic ulcers without an eroded artery in their base), that it is proposed to call them 'pernicious haemorrhage'. These cases are not common; at St. Thomas's Hospital there are about 5 annually, and the diagnosis may be difficult. The cases show a chronic ulcer with an eroded artery in their base, rarely occur before the age of 40, recur, and show a recovery rate of 1 in 4 only. The treatment recommended is partial gastrectomy, excising of the area of ulceration, with 1 or 2 pints of blood transfused during the operation to counteract shock.

New Physical Sign in Perforated Duodenal Ulcer

J. O. Bower claimed to describe a new physical sign useful in the early diagnosis of perforated duodenal ulcer. This is diminished liver dullness, the diminution often beginning a few minutes after perforation, and the usual time for a complete obliteration varying from one to four hours. Associated with this there is usually demonstrable free fluid in the peritoneal cavity. When examining for the sign the patient is placed in the supine position, and the liver area percussed. If only partially obliterated, the exact area of liver dullness is outlined with ink, but in most cases the obliteration will be complete. The patient is helped to turn on his abdomen; after a few minutes he is again turned on to his back, when the area of dullness can be definitely outlined. If this area is repeatedly percussed at short intervals, it will be found that dullness is gradually replaced by tympanites. In acute pancreatitis and high intestinal obstruction, there is no air in the peritoneal cavity. In subacute perforation of the duodenum, and in fulminating appendical perforation, gas is not usually present in sufficient quantity to be of definite importance.

Bower, J. O. (1940) *Amer. J. Surg.*, **48**, 436.

Harman, J. B. (1939) *St. Thom. Hosp. Rep.*, 2nd ser. **4**, 139.

Diagnosis and Differential Diagnosis

Perforation following Barium Sulphate Meal

G. Buttner and W. Iangerau described a case of perforation of a duodenal ulcer after administration of a barium sulphate meal. The perforation occurred at the site of the ulcer, 6 hours after the meal was given; the patient collapsed and died soon after operation. The authors collected the recorded similar case histories and found that such perforations are not at all uncommon, and that they are much more

dangerous than perforations in which ordinary stomach contents escape into the abdominal cavity. The barium meal should be postponed in acute cases and its administration should as a rule be carried through while the patient is under observation in hospital.

Buttner, G., and Fangerau, W. (1939) *Beitr. klin. Chir.*, **170**, 58

Complications

Melaena

Amount of blood necessary to cause tarry stools.—W. A. Daniel and S. Egan investigated the amount of blood required to produce a tarry stool when it was taken by mouth by 10 healthy medical students. Progressively large quantities of venous blood were taken until black glistening faeces appeared. An ordinary diet had been taken. Then 4 students repeated the proceeding, but on a diet of milk and cream to eliminate the possibility that some substance in the usual diet was responsible for the colour of the faeces. From 50 to 80 c cm. of blood was necessary to produce a tarry stool. In 2 of the students on the milk and cream diet, 5 to 10 c cm. more of blood were required to produce it than was necessary on the ordinary diet.

Daniel, W. A., Jnr., and Egan, S. (1939) *J. Amer. med. Ass.*, **113**, 2232

Treatment

Effects of Antacids on Gastric Acidity

J. B. Kirsner and W. I. Palmer investigated the effects of various commonly-used antacids on the hydrogen-ion concentration of the gastric contents in 25 patients with healing duodenal ulcer. The hydrogen-ion concentration of the gastric contents removed hourly was determined by the glass-electrode method. Control studies were made with a general diet and with hourly feedings of a three-ounce mixture of milk and cream. The alkalis, which included calcium carbonate and sodium bicarbonate in varying amounts, calcium carbonate alone, aluminium hydroxide, tri-calsate, tribasic calcium phosphate, and magnesium trisilicate, were given hourly. It was found that the gastric acidity was slightly and temporarily reduced by the administration of food, and that the higher the protein and fat content of milk preparations, the greater was the neutralization of acid. Of the various antacids studied, calcium carbonate, in doses of 2 or 4 g. hourly, was the most effective neutralizer of gastric acidity. Tri-calsate, tribasic calcium phosphate, and magnesium trisilicate in the dosage employed were progressively less effective. Aluminium hydroxide gel exerted relatively little influence on the pH of the gastric juice, though in doses of 3.0 c cm. its neutralizing effect was appreciable. Atropine sulphate, in doses of 1 mg. four times daily by mouth, had no influence on the pH of the gastric contents, though the volume of secretion was apparently reduced. The gastric acidity was most effectively controlled by the use of atropine and calcium carbonate, or with calcium carbonate and sodium bicarbonate. Atropine also permits the effective use of smaller amounts of alkali.

I. Steigmann and B. Fantus investigated the antacid properties of Sippy powder No. 1 (1 part of calcium carbonate and 3 parts of sodium bicarbonate), colloidal aluminium hydroxide, and a neutralized Karaya gum. These preparations were studied on 100 cases of peptic ulcer, by means of fractional test-meals. It was found that all of these agents gave symptomatic relief in a large percentage of cases, without producing a uniform and constant reduction in the gastric acidity. The relief of pain given therefore must have been secured in a different manner than simply by means of an antacid effect. A mixture consisting of bismuth subnitrate and dilute nitric acid was also tried and its effect was similar to that of the antacids.

Colloidal Aluminium Hydroxide

E. S. Emery and R. B. Rutherford also reported the results obtained from the use of aluminium hydroxide in 14 severe cases of peptic ulcer. After these patients had been observed for an average period of 15 months, 8 were found to be symptom-free, and were considered as well. Two were classified as satisfactory, having only had a return of mild symptoms on one or two occasions. Four cases were not

satisfactory, one having difficulty in taking the drug, one having had a massive haemorrhage, and 2 having had a return of active symptoms. The satisfactory patients took aluminium hydroxide every hour throughout the day for 4 or 5 months, thereafter they were given milk once between each meal and aluminium hydroxide 5 or 6 times a day. The authors concluded that, in view of the severity of the cases, the results were very satisfactory.

J. F. McIntosh and C. G. Sutherland employed colloidal aluminium hydroxide in 38 cases of peptic ulcer, out of which there were only 4 definite failures. One group of 7 out-patients comprised 6 cases of duodenal ulcer without complications and one of jejunal ulcer, all proved by X-ray examination and showing evidence of active ulceration. These patients were allowed to follow their normal occupations throughout the course of treatment. In some, frequent feedings were advised, with milk given freely as in interval feeding. As improvement occurred, three regular meals were instituted. Aluminium hydroxide was given, usually in 2-drachm doses, at first 6 times a day, and later, as improvement occurred, 2 or 3 times a day. All of these cases did well, and in 5 radiological examination, carried out some time later, showed the ulcer to be healed. A second group of 19 ward cases comprised 15 of duodenal and 4 of gastric ulcer, most of the cases being of long standing, while a third group consisted of 9 cases of duodenal ulcer and one of gastric ulcer, all with gross haemorrhage. A further group comprised two cases of duodenal ulcer, one complicated by chronic paranasitis. With the exception of the latter two cases, most of the patients in the above groups responded well to aluminium hydroxide. The authors concluded that aluminium hydroxide offers many advantages over the older antacids. They considered that it is most effective when taken shortly before eating. They raised the question as to whether there is any need for the use of diets of the Sippy type, with consequent under-nutrition, when aluminium hydroxide is employed. There appears to be good evidence that frequent small feedings are an undesirable stimulus to gastric secretion. They considered that, if sufficient aluminium hydroxide is given, a much more generous and less troublesome dietary can be employed.

Intra-gastric drip method. E. I. Woldman and C. G. Polan investigated the value of colloidal aluminium hydroxide in the treatment of 407 consecutive cases of peptic ulcer. The aluminium hydroxide is diluted to 25 per cent and continuously dripped into the stomach through a naso-gastric tube, at the rate of 15 drops per minute, day and night, for 10 days. With this treatment there is given a bland diet, in small quantities every 2 hours for 12 hours. Small blood transfusions are given if the systolic blood-pressure drops below 90, or if the haemoglobin falls below 30 per cent. After this treatment the patient is dismissed from hospital and continues to take 2 teaspoonfuls of the aluminium hydroxide in 2 ounces of water every 2 hours until bedtime for 30 days. He is also placed on a convalescent diet. This treatment is efficacious because the continuous action of the hydroxide prevents too much acid being formed and destroying the healing processes. The hydroxide also provides a jelly-like covering to the ulcer and gives it added protection.

In all the cases pain was relieved in 24 hours. The ulcers healed very rapidly even in those patients who had not responded to other forms of treatment. In 101 patients with large haematemeses only 3 died under this treatment. Chronic cases who have taken the treatment for 2 years or more have been free from symptoms although they had previously had frequent attacks of pain. There are no harmful effects from taking the drug for so long periods.

J. I. Lads treated 40 cases of peptic ulcer with colloidal aluminium hydroxide gel by the continuous intra-gastric drip method. The colloidal compound was mixed with water in the proportion of 1:3 and dripped through the tube at a rate of 15 to 20 drops per minute both day and night. The patient was confined to bed on a light diet, 18 patients had the continuous drip for 7 days, 11 for 10 days and 10 for 14 days. Subsequently aluminium hydroxide was given by mouth in conjunction with dietary modifications. This was continued until clinical and radiological evidence demonstrated a complete cure. Of the 40 patients treated in this way, 38 were completely relieved of pain, 26 of them within 12 hours. Of 6 patients with gastric or duodenal haemorrhage, 5 ceased bleeding within 48 hours. Reduction in the hydrochloric acid of the stomach commenced within one hour, and by the third or fourth day no free hydrochloric acid was present.

Magnesium Trisilicate

M Kraemer and B Aaron carefully investigated magnesium trisilicate in 90 cases of peptic ulcer, 5 being gastric ulcer, 1 marginal, and 84 duodenal. The duration of ulcer symptoms for the group varied from 1 month to 30 years with an average of 9½ years. The ages varied from 17 to 77 years. The cases were followed up from 3 to 20 months. Two of the patients had had acute perforations, and several had had severe acute hemorrhages. In most cases treatment was ambulatory. The powder was given in 1 g doses, six times daily. A mixture containing bromide and tincture of belladonna was given before the three main meals. Patients with night pain took a glass of milk and 1 g. of the trisilicate at intervals during the night. All patients were gradually placed on three meals per day with occasional milk feedings at 4 p.m. and at bedtime, and the number of powders taken per day was progressively reduced, so that, within 3 to 6 months, many of the patients had discontinued taking the powder. All patients were advised to refrain permanently from tobacco, condiments, excess roughage, and alcohol. In 17 patients the use of magnesium trisilicate did not prove entirely satisfactory. Of these 6 had recurrences which were promptly cured by resumption of treatment. Eleven patients were not benefited by the treatment. Of 86 cases in which successful medical treatment could have been anticipated, this powder was used exclusively in 79, or 92 per cent. Seventy-three patients (84 per cent) were entirely freed from symptoms and had no untoward effects of any kind for from 3 months to over 1½ years. Dosage as large as 12 g per day produced no change from normal in the CO_2 -combining power of the blood. The drug had no effect on colonic mobility, and had no discernible toxic effects.

Injection of Progynon

W Schulz mentions previous experiments with female sex hormone in ulcers of the stomach and intestine (Korbsch) and records the effect in 7 of his own cases, in which 10,000 units of progynon were injected every second day, the dose being in later cases reduced to 1,000 units and to 500 units. The symptoms were relieved after 8 to 14 days of treatment, gastroscopy showing that the ulcers had disappeared. In the patients who received too large doses of progynon, pain and a feeling of repletion appeared after the treatment, due to hyperaemia of the gastric mucosa. The author recommends fractional injection of small doses. Progynon probably produces its effect by a dilatation of the capillaries and hyperaemia of the gastric mucosa, and should therefore be specially effective in ulcers caused by spasm of the capillaries.

Posterior-Pituitary Powder Insufflation

Believing that the posterior lobe of the pituitary gland plays an important role in the causation of peptic ulcer, M H Metz *et al* treated 76 cases by intranasal insufflation of posterior-pituitary powder. About ½ gram was insufflated four times a day, the tip of the insufflator being inserted one-half inch into the nostril. This dosage was given for 5 to 6 weeks, then reduced to half for 2 more weeks. Patients were not confined to bed nor was their dietary substantially modified. While oral administration of the powder in capsule or compressed tablet form proved ineffective, insufflation was of considerable value in 67 of the 76 cases, favourable results being secured in a period ranging from 3 to 9 weeks. There was relief of pain, gain in appetite, weight, and strength, and disappearance of the ulcer in at least 15 cases. This method of treatment must be considered as complementary to the accepted principles of peptic ulcer management.

Histaminase

P O'Hollaren reported a case of peptic ulcer treated with histaminase. The patient had a history of peptic ulcer of 8 years' duration. He had previously been treated by diet and antacid therapy. He was placed on histaminase treatment, 20 units of the drug, 3 times daily before food. He continued on an ordinary diet, took alcohol and smoked heavily. After 2 days the symptoms began to subside, and in 20 days he was symptom-free. He then began to reduce the dosage by 10 units a day, until a maintenance dose of 10 units a day was reached. There had been no recurrence of symptoms at the time of the report.

Renal Calculi following Alkaline Therapy

T. Moore stated that the most important measure in the treatment of peptic ulcer is small frequent meals and not the giving of large quantities of alkalis. Moreover, large amounts of alkali may be definitely harmful in that urinary calculi may arise from their use. The urine of these patients becomes thick with phosphatic deposits and phosphatic calculi may develop, usually in the inferior calyx. He reported 2 cases of renal calculi, one successfully removed at operation, and the other in the ureter being passed spontaneously, following the ingestion of large quantities of alkali. The phosphates are deposited because the alkali raises the pH of the urine.

Surgical

O. T. Clagett analyses 272 (males 220, females 52) consecutive cases of chronic gastric ulcer operated upon at the Mayo Clinic during 1933-7. A questionnaire was recently sent to all the patients. The results were very good, only one patient did not improve after the various operations carried out, there was not any history of later haemorrhage or of gastro-jejunal ulcer. There were 16 deaths, or 5.9 per cent, the average age of these patients being 59 years, an age with a greater risk than in earlier age from surgical treatment; post-operative pneumonia was responsible for 10 of the 16 fatalities; one death was due to pulmonary embolism, one to coronary thrombosis, one to peritonitis, one to duodenal fistula, and 2 to post-operative haemorrhage. The operation most often performed, in 131 cases, was the posterior Polya type of partial gastric resection, the anterior Polya-Balfour operation was done in 9 cases. The results of these were very successful for the 85 patients who answered the questionnaire, there was an average gain of 13 lb. in weight, 80 were in excellent health, and 5 were in very good health and had only slight occasional discomfort. The advantages of the Polya resection are that it removes the lesion and provides the maximal protection against recurrent ulceration. It may, however, not be advisable when the lesion is so high that resection is technically impossible, or the patient's condition does not justify such an extensive operation. Billroth I resection, employed only for ulcers in the pyloric third of the stomach and when the duodenum was large and mobile, was performed on 22 patients, 9 of whom answered the enquiry; 8 were free from symptoms, and one had occasional slight discomfort. Excision of the ulcer by knife or cautery combined with gastro-enterostomy was carried out on 50 patients, 29 of whom reported later, there was an average gain of 12 lb., and 2 only had slight distress occasionally. Out of 9 patients who reported after knife or cautery excision alone, 5 were completely relieved, and showed an average gain of 15 lb. in weight. Gastro-enterostomy alone, like the last operation when there was a good reason against excision, was reported by 15, one only having mild discomfort. Pyloroplasty with excision was performed on 9 patients, 4 of whom replied that they were in good health. Commenting on this series, W. Walters said that for 15 years simple excision of an ulcer has been considered the least satisfactory of surgical procedures for gastric ulcer unless it is combined with some measure that will assist in lowering the acidity of the gastric contents and will increase the rapidity of the stomach in emptying.

Clagett, O. T. (1940) *Proc. Mayo Clin.*, **15**, 337.

Lads, J. I. (1940) *Amer. J. digest. Dis.*, **7**, 14.

Emery, F. S., and Rutheford, R. B. (1940) *New Engl. J. Med.*, **222**, 205.

Kirsner, J. B., and Palmer, W. L. (1940) *Amer. J. digest. Dis.*, **7**, 85.

Kracmer, M., and Aaron, B. (1940) *Amer. J. digest. Dis.*, **7**, 57.

McIntosh, J. F., and Sutherland, C. G. (1940) *Canad. med. Ass. J.*, **42**, 140.

Metz, M. H., Lackey, R. W., Wigby, P. F., and Patterson, C. O. (1940) *Amer. J. digest. Dis.*, **7**, 14.

Moore, T. (1939) *Lancet*, **2**, 1118.

O'Hollaren, P. (1940) *Northw. Med.*, *Seattle*, **39**, 216.

Schulz, W. (1939) *Med. Klinik*, **35**, 914.

Steigmann, F., and Fantus, B. (1940) *Amer. J. digest. Dis.*, **7**, 197.

Walters, W. (1940) *Proc. Mayo Clin.*, **15**, 339.

Woldman, F. E., and Polan, C. G. (1939) *Amer. J. med. Sci.*, **198**, 155.

PERITONITIS: ACUTE PERITONITIS

See also B.E.M.P., Vol. IX, p. 537, and Cumulative Supplement, Key No. 1241

Diagnosis and Differential Diagnosis

Diagnosis of Peritonism

J. M. Waugh contributes a note on the differential diagnosis and treatment of peritonism or traumatic peritonitis, which has been defined as the reflex production of the symptoms usually associated with severe damage of the abdominal viscera, such as perforation and intra-peritoneal haemorrhage. Differential diagnosis is specially important because operation should be avoided in peritonism. At the Mayo Clinic the most frequent causes of peritonism are fracture of the ribs, spinal column, or pelvis. The pain, tenderness and rigidity are the same in both conditions. After 1 or 2 hours of observation, during which treatment for shock is carried out, the shock in peritonism disappears and the physical signs tend to diminish in intensity, whereas in peritonitis the signs more often than not become more severe. When rupture of the stomach or intestine has occurred a plain X-ray taken with the patient standing up may show a bubble of gas under the diaphragm, and thus indicate laparotomy, whereas evidence of fractures of the ribs, spine and pelvis would explain the symptoms and make the surgeon hesitate to operate unless persistence of physical signs render it probable that an additional intra-peritoneal lesion is also present. In peritonism elevation of the foot of the bed and external heat may improve the blood-pressure and pulse, though it must be borne in mind that transfusion may cause such a temporary improvement in an intra-peritoneal catastrophe. In fracture of the pelvis, the presence of blood in the urine is an important sign.

Waugh, J. M. (1940) *Proc. Mayo Clin.*, **15**, 319.

Prophylaxis

Use of Whole Blood

L. G. Joseph was struck by the fact that, in many emergency coeliotomies performed on cases of abdominal wounds, the patient recovered, whereas the usual carefully conducted resection of the large bowel so often ends with a fatal peritonitis. He felt that the presence of blood in the cases of abdominal wounds had possibly a beneficial effect. He therefore conducted experiments in animals in an attempt to substantiate the theory that fresh blood is capable of augmenting the natural defence mechanism of the peritoneum. He found that, in almost 100 per cent of cases, infection of the peritoneal cavity with a small quantity of fresh faeces did not of itself tend to produce peritonitis, but that infection of the peritoneal cavity with a small quantity of fresh faeces together with exposure and trauma to the bowel wall tended to produce peritonitis in 90 per cent of cases. The injection of free blood into the peritoneal cavity increased the immunity of the peritoneum against infection by over 75 per cent, and prevented the production of adhesions in a large percentage of cases.

Joseph, L. G. (1940) *Ann. Surg.*, **111**, 618.

Primary Peritonitis in Children

Treatment

Surgical and chemotherapeutic—W. E. Ladd *et al.* discuss primary peritonitis in infants and children. The condition is usually pneumococcal or haemolytic streptococcal in origin, and most common in the first 4 years of life, the sexes being about equally affected. The patients are usually severely ill with fever, abdominal pain, nausea, and vomiting. As soon as the diagnosis is made the organism responsible must be determined. Drainage of the peritoneal cavity as soon as possible is advocated, and the patient should be given plenty of fluids and frequent small blood transfusions. If the condition is due to the haemolytic streptococcus, sulphanilamide

should be prescribed, and if to the pneumococcus, sulphapyridine and specific serum of the proper group should be given

1 add, W. L. Botsford, T. W., and Curnen, F. C. (1939) *J. Amer. med. Ass.*, **113**, 1455

PHARMACOLOGY

See also Surveys and Abstracts 1939, p. 471, and p. 127 of this volume

Action of Drugs

In a thought-stimulating address, 'How Do Drugs Act?' Langdon-Brown covers a wide field, and on modern lines; it recalls the *Lectures on the Actions of Medicine* (1897) by his predecessor, Lauder Brunton, at St Bartholomew's Hospital. The notion that vegetable products are relatively harmless and the most 'natural' for animals is criticized in favour of the view that this position should be held by their own hormones and antitoxins. After a plea for empiricism, as illustrated by the remedy cinchona used for nearly 200 years before the isolation of quinine, the principal ways in which drugs act are discussed, namely (i) by increasing or diminishing the effects on the cell of external stimuli, with examples of hormones, adrenaline and acetylcholine, and of drugs, such as prostigmin and the barbiturates, (ii) by modifying the chemical changes within the cell, as illustrated by the action of thyroxine and vitamins, such as ascorbic acid, and (iii) by alteration induced in the chemical composition of medicaments by the cells so as to give rise to substances capable of fresh activity yet with less toxicity, as shown in chemotherapy, for example the sulphonamides and the organic mercurials.

Langdon-Brown, W. (1940) *Pharm. J.*, 4th ser. **90**, 103, 119

Relation between Age and Weight and Dosage of Drugs

With regard to the relation between age and weight and the dosage of drugs, W. I. Dawson concludes that there is no quantitative rule available at present, or likely to be in the future, that will apply to all drugs, and that the dosage for children of some important drugs differs much less from the adult's than would be expected on the basis of a direct proportion to body weight. The only principle of dosage indeed available is that the dose must be adjusted to the individual patient, and that nothing can, or will, supersede clinical experience, and careful study, combined with good judgment. On the basis of clinical observation the therapeutic dosage of atropine, the arsphenamines, bismuth, digitalis, mandelic acid, some mercurials, sulphonamides and other drugs has been set at a somewhat higher level in proportion to weight for infants and children than for adults. On the other hand the dosage of morphine and strychnine, even in direct proportion to body weight, appears to be too high for safety in some individuals, and caution until susceptibility has been determined should be maintained, at least in infants, children, and the aged. The greater tolerance of the young for some drugs may be due to various factors, possibly including proportionately larger average surface area, basal metabolic rate, liver weight, and daily urinary volume.

Dawson, W. T. (1940) *Ann. intern. Med.*, **13**, 1594

Application of Drugs in Emulsion

P. Heath draws attention to the unequal pupillary response, and unequal effects on accommodation, of single dosages of drugs in aqueous solution, the use of emulsions is recommended. The variable response to aqueous solutions may be due to the winking out of the solution, irritability from pH above or below normal, high surface tension, the relatively strong bond between drug and base, the state of the conjunctival secretions, unequal lacrimal drainage, dilution and other causes. Ointments have not proved satisfactory owing to unequal absorption of the drug from the base and the unequal application and dosage, the corneal obscurity from the oil film has disturbed anterior-segment examinations. Some trend toward uniform response follows the use of a drug in buffered solutions, gelatin disks, multiple dosage oleaceous bases, and after local anaesthesia. The author remarks that an emulsion has not been used as a vehicle in ophthalmology although it has been used on other

mucous membranes. The ophthalmic drug in a vehicle consisting of an emulsion permits most uniform dosage, acts over a longer time, is more tenacious, does not wink out, and has a low surface tension. The visibility of the drop is high, it is easy to apply, and the drug mixes readily with the ocular secretions. An emollient effect is produced; the size of dosage is relatively constant, a wider range of pH is possible without irritation, and stability is high. The drops may be made mildly antiseptic and still non-irritating. The use of an emulsion does not interfere with anterior-segment studies.

The author states that the most effective emulsion is the water-in-oil type with the active ingredient in the aqueous phase, the preparation should be put through a colloidal mill. The author reports that he has adopted neo-synephrin hydrochloride as a sympathetic drug after animal and clinical tests have demonstrated its relatively longer, stronger, and more uniform action.

Heath, P. (1939) *Amer. J. Ophthalm.*, **22**, 904

Action of Various Drugs on the Nasal Mucosa

A. W. Proetz investigated the action of certain drugs on the nasal mucosa. The studies were made on living animal membranes in situ, and on extirpated mucosa from animals and man. The nasal cilia were observed microscopically in each case. Benzedrine sulphate, with and without oil of lavender, by inhalation produced no appreciable change in the amplitude or rapidity of the ciliary beat. The same drug applied directly stopped all ciliary action instantly. With 1 to 3 per cent solutions slowing and cessation occurred in appropriate times. Alcohol, not unnaturally, stopped all ciliary action, though the mucosa would recover after treatment with a 5 per cent solution. 'Wetting agents', capable of reducing surface tension, were applied. Decylbenzene sodium sulphonate in a 0.1 per cent solution was rapidly fatal to the mucosa. The same was found with monobutyl-diphenyl sodium monosulphonate and monobutyl-phenyl phenol sodium monosulphonate. The effect of ether vapour was considered. It produced no permanent damage to the cilia, although the fluid itself was rapidly fatal to the mucosa. Chloroform produced similar results. Nitrous oxide had no effect on the cilia. Cold, produced by a blast or by the evaporation of ether, had a temporary inhibiting effect upon the cilia.

Proetz, A. W. (1939) *Arch. Otolaryng.*, Chicago, **30**, 509

Oligoseptic Treatment of Ocular Infections

L. I. Hallay describes the oligoseptic treatment of ocular infection. The term 'oligosepsis' was introduced to describe any chemotherapy aimed at reducing the infective capacity of pathogenic organisms without destroying them. It was based upon results of experiments by Much that harmless parasites can be made extremely virulent by treatment with acids and upon the author's own experience that in actual infection pathogenic micro-organisms can be rendered harmless by restoring the acid-base balance in the infected area. This appeared to be possible: (a) by hydrotherapeutic procedures designed to produce sweating, (b) by antiketogenic diet, (c) by application of powdered sodium bicarbonate or soap lather as buffers in infections of the skin; (d) by application of protein buffers in infections of mucous membranes. Further development of these ideas led the author to evaluate the buffer properties of soap lather in the oligoseptic treatment of ocular infections. According to present knowledge, soap solutions undergo very little electrolysis and the alkalinity of soap when used for washing can be ignored. The infinitesimal degree of ionization of soap-solution seems to explain the buffer action of soap when applied to infected areas of the skin, and the buffer-like action of soap lather in wet media, especially in the eye.

The author first used soap lather in an ocular condition on himself. He sustained a traumatic injury of the right eye and eyeball, associated with subconjunctival bleeding and extensive reactive conjunctivitis. The application of soap to the eye caused a considerable increase of pain due to trauma; this eased in a few minutes and the eye, which had been closed since the previous day, opened spontaneously. There was a marked increase of the injection of the conjunctival capillaries, this disappeared in half an hour, leaving a bright-red spot on the cornea due to the subconjunctival

bleeding. The treatment was repeated next morning and resulted in complete recovery. Later, the author corroborated this result in numerous industrial accidents.

The treatment was further applied to cases of conjunctivitis or keratitis due to infection. Simple cases of acute conjunctivitis or keratitis resulted without exception in complete recovery. An incipient conjunctivitis would clear up in half an hour, in cases that had persisted for more than a day, a daily application for several days was necessary. The prodromal conjunctivitis of measles seemed to clear up temporarily after soap-lather application. In an epidemic of 32 cases of acute contagious conjunctivitis, most of them were treated by oligosepsis. The same progress was observed in several cases of blepharo-conjunctivitis; this stubborn condition was sometimes cured by systematic treatment with the buffer. The reaction of hordeola to oligosepsis depended upon the stage of their development. In an early stage they could be checked by a single application; suppurating hordeola had to be punctured and the pus removed before application of the soap lather. Two cases of dacryocystitis reacted favourably. The treatment was applied to a case of ophthalmia neonatorum, seen 3 weeks after birth, in which a marked ophthalmoblenorrhoea had been present since the third day postpartum. The baby was cyanotic and both conjunctival sacs were filled with pus. Both eyes were washed out with soap and water and the soap buffer was applied, this caused considerable pain but after several minutes the baby opened its eyes and showed signs of relief. Oligoseptic treatment was repeated each morning for 6 weeks and resulted in complete recovery, with no remaining injury to the eyes.

Hallay, L. I. (1939) *Amer. J. Ophthalm.*, **22**, 1012.

Much, H. (1921) *Dtsch. med. Wschr.*, **47**, 321.

Acetylsalicylic Acid

Stability

H. W. Tomski and L. J. Waller report their investigation on the loss of acetylsalicylic acid in saturated alcoholic and acid alcoholic solutions as well as in suspensions, and conclude that (i) acetylsalicylic acid (3 per cent) when dissolved in 50 per cent alcohol and kept under ordinary laboratory conditions, loses about 1.5 per cent daily, 6.0 to 6.5 per cent a week, and 13.5 to 14.5 per cent in a month. A suspension of the same strength and kept under the same conditions loses 0.3 per cent daily, 1.6 to 2.0 per cent weekly, and 7.0 to 8.0 per cent monthly; (ii) suspensions should therefore be prescribed and dispensed, instead of in solutions containing ammonium acetate or potassium citrate when the administration of tablets is undesirable.

Tomski, H. W. and Waller, L. J. (1940) *Pharm. J.*, 4th ser., **90**, 53.

Adrenaline

Anticonvulsant Effect

I. Gellhorn *et al.* investigated the effects of adrenaline upon insulin and cardiazol (leptazol) convulsions in rabbits. Very small quantities (0.004 to 0.015 mg. per kilogram of body weight) of the drug injected intravenously inhibited the convulsions. A rabbit narcotized with soluble barbitone can be awakened by an injection of metrazol, adrenaline injected afterwards causing the rabbit to go to sleep again. The drug would therefore, in minute doses, appear to be an anticonvulsant. It is, however, possible to increase the convulsant action of metrazol with adrenaline, provided the dose is high enough. Experiments with cats showed that the anticonvulsant action of adrenaline is due to its action on the carotid sinus and depressor reflexes. The presence of either of these two mechanisms is sufficient to produce this effect. The authors suggested that epilepsy might be due to an adrenaline blood-level which was below normal, or to the possession of a somatic nervous system which was less sensitive to its action. They suggested that quantitative estimation of the adrenaline in the blood might be made in epileptics.

Related Compounds

J. A. Gunn discussed the therapeutic uses of compounds related to adrenaline with the object of finding improved substitutes for the drug. Adrenaline, given intraven-

ously, produces a sudden sharp rise of blood-pressure, intramuscularly the rise is less pronounced, and there is little or no effect when given subcutaneously. The drug is inactive given by mouth. In the treatment of shock, since adrenaline acts on the arterioles and only produces a transient rise of blood-pressure, and the main condition is dilatation of the capillaries, the drug is of little use. An allied drug, veritol, however, produces a much more sustained rise. The drugs of this group have a stimulating action upon the heart, causing it to beat more quickly and may therefore be of value in this condition. This reaction occurs through stimulation of the sympathetic nerve supply, and adrenaline is the most efficient drug in the group for this purpose. It has another action in that it antagonizes some cardiac depressants such as chloral hydrate. Adrenaline can also be used to restore rhythmic contractility to an arrested heart. Adrenaline produces a local vasoconstriction which is useful in surgery and it also prolongs local anaesthesia by preventing the absorption of the anaesthetic. A serious disadvantage in these cases is that it increases the toxicity of cocaine applied locally. Allied drugs such as ephedrine and corbasil (norephedrine) are better for use as vasoconstrictors than adrenaline. As an eccholic adrenaline is not very satisfactory, because its action on the uterine muscle is only transient and the rise of pressure it produces encourages haemorrhage. Some workers have found it, in certain concentrations, to relax and not contract the muscle. Related compounds, such as tyramine are better, since they produce a more prolonged contraction of the uterus and a smaller rise of blood-pressure. Adrenaline given hypodermically is the best compound for relaxing the bronchi in asthmatic attacks. Ephedrine has the advantage that it can be given by mouth, but it is rather less effective. Adrenaline does not stimulate the central nervous system but related compounds such as ephedrine and benzedrine do. They affect mainly the motor cortex and the respiratory centre. The drugs may be used to antagonize certain central nervous system depressants such as chloral hydrate, and in the treatment of nervous depression. Adrenaline has some action on voluntary muscle and has been used in some cases of myasthenia gravis. Ephedrine, tyramine, and dihydroxyphenylethylamine have been found more efficacious in this disorder. In nocturnal enuresis ephedrine acts by contracting the sphincter and the trigone of the bladder. Benzedrine produces relaxation of the pyloric sphincter and the smooth muscle of the gastro-intestinal tract. It is therefore useful in abolishing spasm. Adrenaline has been recommended to stop haemorrhage from a gastric ulcer but it has the disadvantage that its action is transient and after constricting the vessels it dilates them.

Effect in Producing Leucocytosis

The subcutaneous injection of adrenaline produces leucocytosis, resulting from action of the leucopoietic system in the bone-marrow or spleen. The question is not settled as to whether the injection of adrenaline produces its effect by stimulating directly the leucopoietic system. C. H. Behr examined 61 patients suffering from various organic affections of the nervous system after injection of adrenaline; in 25 patients leucocytosis did not ensue. Consequently it would appear that adrenaline produces its effect through a regulating centre in the mid-brain, but not by a direct effect on the leucopoietic system. Therefore a negative result of the adrenaline test suggests a diagnosis of disturbance in the mid-brain, whereas a positive result does not demonstrate absence of disturbance in the mid-brain.

Neurotic Symptoms and Changes in Blood-Pressure

S. H. Krames and I. C. Sherman compared the effects of adrenaline on the blood-pressure and pulse-rate of psychoneurotic and normal persons, and compared the subjective sensations following the injection to those recorded in the patient's clinical notes. Twenty-five psychoneurotics and 19 normals were investigated. The patients were rested until the pulse and blood-pressure had reached a stable level as shown by frequent readings, then 0.5 c.cm. of physiological saline was injected into the cubital vein for control observations. Readings were then taken again until they were stable. This always occurred in less than 10 minutes. The procedure was then repeated using 0.01 mg. of adrenaline for the injection. After both injections the patients were asked to give an account of their subjective symptoms. In all cases the reaction to the saline was not so great as the reaction to the adrenaline. There was no constant change in the pulse-rate or blood-pressure. Subjective psychoneurotic

symptoms were produced in both the psychoneurotic and normal persons. The psychoneurotic often recognized an exacerbation of his symptoms, and latent neurotic symptoms were sometimes brought to light. By discussing the symptoms following the injection, it was shown to the patient that his psychoneurotic symptoms were not imaginary, but had a physiological basis.

Hypersensitivity

A. E. Cohen and M. I. Waterstone reported 2 cases of hypersensitivity to adrenaline. No reagins could be demonstrated in the serum of either patient. Both cases showed a characteristic necrosis following the subcutaneous and intradermal injections of adrenaline, whereas neither showed sensitivity to synthetic adrenaline hydrochloride. One case was particularly interesting because the patient developed such a high degree of immunity to the usual adrenaline preparations, that she obtained little or no relief from their use.

Behr, C. H. (1939) *Nervenzzt.*, **12**, 489.

Cohen, A. E., and Waterstone, M. I. (1940) *J. Allergy*, **11**, 393.

Grellhorn, L., Darrow, C. W., and Yesnick, I. (1939) *Arch. Neurol. Psychiat.*, Chicago, **42**, 826.

Gunn, J. A. (1939) *Brit. med. J.*, **2**, 214.

Kraimes, S. H., and Sherman, I. C. (1940) *J. Amer. med. Ass.*, **114**, 843.

Aminophyllin

R. I. Levy *et al.* investigating the effects of certain drugs upon the effects of induced anoxaemia in patients with coronary insufficiency, came to the following conclusions. Aminophyllin, given intravenously, in doses of 0.48 g., caused a prolongation of 63 per cent in the time of appearance of pain. The RS-T deviation was diminished by 58 per cent. The T waves were modified in 7 out of 10 cases. When taken by mouth the drug caused a prolongation of 26 per cent in the time of appearance of pain. Nitroglycerin caused a prolongation of 51 per cent in the time of appearance of pain. RS-T deviation was diminished by 47 per cent.

Levy, R. I., Bruenn, H. G., and Williams, N. F. (1940) *Amer. Heart J.*, **19**, 639.

Amyl Nitrite

Effect on Bronchial Tree

W. F. Nicholson investigated the effect of amyl nitrite on the bronchial tree, as the drug is so often used to prevent the dyspnoea of bronchial asthma. The action was investigated in both dogs and man. Dilatation of the bronchi was produced in man. The younger the patient and the smaller the bronchiole, the greater was the dilatation. The latter observation is due to the fact that the smaller bronchioles contain proportionately more smooth muscle, and are therefore able to dilate more readily. Nicholson suggested that nitrites might be used in the early stages of bronchiectasis to procure dilatation and subsequent drainage and to prevent repeated bronchoscopy. Amyl nitrite might also be used in acute massive collapse to help aerate the lung and also obviate the necessity for bronchoscopy. Nicholson also suggested that the amount of dilatation produced by amyl nitrite could be used to diagnose the degree of bronchial stenosis.

Nicholson, W. F. (1939) *J. thorac. Surg.*, **9**, 194.

Atropine and Ergotoxine

Antidotes to Scorpion Toxin

The demonstration by Mohammed that the toxin of the scorpion acted as a powerful stimulant, led A. Hassan and A. H. Mohammed to investigate the effect of paralytics of the sympathetic and parasympathetic nerves, such as ergotoxine and atropine, on animals poisoned with scorpion toxin. They found that subcutaneous injection of either drug in the poisoned rat, although it did not abolish the symptoms, saved the animal from certain death. The effect of both drugs together, 1.6 mg. of atropine and 0.24 mg. of ergotoxine, gave an even better result. It saved the lives of rats injected with 3 times the minimal lethal dose of the toxin. This

antidote saved the lives of 3 out of 3 rats 20 minutes after the toxin had been injected and of 2 out of 3 rats 90 minutes after. Dogs could only be saved by a combination of the drugs and not by one alone. It was also impossible to save them if they had received more than 2 minimal lethal doses. The authors suggested that these two drugs should be used in the treatment of scorpion stings in man.

Hassan, A., and Mohammed, A. H. (1940) *Lancet*, **1**, 1001

Atropine, Scopolamine, and Homatropine-Paredrine

Effect on Pupil

J. Marron investigated the cycloplegic and mydriatic actions of atropine, scopolamine, and homatropine-paredrine. The corrected vision in both eyes of the subjects investigated was at least 1.2 D. The age of those receiving atropine ranged from 15 to 40 years. A 1 per cent solution was instilled and 4 drops produced a maximum diminution in the range of accommodation. The accommodation recovered fully in 18 days, but most of the subjects could read by the third day. The pupil first constricted, probably due to irritation, but was fully dilated after 40 minutes. This dilatation was maintained throughout atropinization and returned to normal 12 days after it ceased. Those receiving scopolamine were aged 15 to 37 years. This drug acted very quickly, the range of accommodation being as low as 1.6 D after 40 minutes. The subjects could read on the third day and the normal range recovered in 10 days. Full mydriasis was produced in 20 minutes and lasted for at least 90 minutes. The pupil returned to normal in 8 days. The homatropine-paredrine combination was given to subjects from 17 to 57 years of age. Maximum diminution in accommodation was reached after 50 minutes. After 6 hours the subject could read and the accommodation was normal after 48 hours. Maximum dilatation of the pupil occurred in 30 minutes, remained fixed for 1 hour, and returned to normal in 48 hours.

Marron, J. (1940) *Arch. Ophthalmol.*, **23**, 340

Benzedrine

Effects of Inhalation on Circulation

C. M. Peters and J. M. Faulkner investigated the effect of benzedrine in the form of the inhalant, with special reference to its effect in heart disease. Ten patients with normal hearts, 57 with various forms of heart disease, and 28 with angina pectoris were investigated. Doses larger than therapeutic doses were given and they had no effect upon the pulse or blood-pressure of any of the patients. There was an occasional small change in the electrocardiograms which was considered of doubtful significance. In one of the patients suffering from angina pectoris the drug appeared to precipitate an attack. It was therefore concluded that this is the only type of heart disease in which the inhaler is contra-indicated as it may precipitate an attack.

Effect on Metabolism and on the Cardiovascular System

K. H. Beyer showed that benzedrine sulphate given orally in doses of 30 mg increased the normal metabolic rate by an average of 15.4 per cent within the first 2½ hours. The rate did not return to normal, as compared with control experiments, for over 9 hours, but returned to normal within 24 hours after administration of the drug. This effect, together with the anoxia so often observed, would appear to be a factor in producing the loss of weight, especially in obese individuals, following the use of benzedrine. The maxima of blood-pressure effects were reached in 1½ hours, after which there was a slow decline in pressures reaching the original levels within 24 hours.

Effect of Large Doses for Long Periods

W. Bloomberg studied the effects of large doses of benzedrine sulphate over long periods in 3 patients; in 2 cases 70 mg or more of the drug had been taken daily for 2 years and 8 months, and in one case for one year and 8 months. No significant deviation from normal, as a result of this massive dosage, was found in any case by clinical or laboratory investigation, and no evidence of addiction or habit formation could be detected.

Beyer, K. H. (1939) *J. Pharmacol.*, **66**, 318

Bloomberg, W. (1940) *New Engl. J. Med.*, **222**, 946

Peters, C. M., and Faulkner, J. M. (1939) *Amer. J. med. Sci.*, **198**, 104

Benzedrine and Paredrine

Pressor Effect

A. Iglaue and M. D. Altschule investigated the pressor action of benzedrine and paredrine. This action, which is marked, is due to arteriolar vaso-constriction. These drugs exhibit their usual pressor effects in patients in whom the vasomotor nerves of most of the body have been paralysed by means of intraspinal procaine or procaine. Hyperventilation, which causes a marked decrease in arterial-blood carbon-dioxide concentration, does not inhibit the pressor action of these drugs. These observations amplify other evidence indicating that the smooth muscle of the arterioles is the site of the pressor action of these drugs.

Iglaue, A., and Altschule, M. D. (1940) *Amer. J. med. Sci.*, **43**, 359

Colloidal Silver and Mercury Ointment

In Venereal Prophylaxis

I. I. Lubowe *et al.* investigated the germicidal properties of a colloidal silver and mercury ointment for use as a prophylactic of venereal disease. Two ointments were tested, the one containing 0.05 per cent colloidal silver, and the other 0.05 per cent colloidal silver with 0.05 per cent colloidal mercury, both of these ointments had a glycerin stearate-cholesterol base. These ointments were tested bacteriologically and experimentally for toxicity. They were found to be definitely gonococcicidal and spirochaetocidal, and to be free from toxic effects.

Lubowe, I. I., Landau, I., and Miskin, D. (1940) *Urol. cutan. Rev.*, **44**, 286

Congo Red

Toxicity and General Effects

Since Congo red is being used more and more as a diagnostic and therapeutic agent, A. P. Richardson and J. R. Dillon investigated its toxicity and general actions. Experimenting with animals they found that the fatal dose in pigeons, rats, rabbits, and cats varied from 150 to 250 mg. per kilogram body weight in the majority of the animals. These amounts were given intravenously and, since very small doses are given thus for diagnostic and therapeutic purposes, the dye would appear to be safe. Congo red stimulated smooth muscle and increased the cardiac muscle tone in these animals. When toxæmia occurred it was characterized by general depression and collapse. Death from Congo red poisoning was due to circulatory failure. The dye was more toxic in saline than in dextrose solution.

Richardson (1939, a) then investigated the absorption, distribution, and sojourn of the dye in the blood. He found that intravenous injection of Congo red produced higher concentrations in the blood of pigeons and rabbits than intramuscular or intraperitoneal injection. The dye disappears from the blood at a constant rate after intravenous injection and after 24 to 72 hours only traces remain. After the dye has disappeared from the blood it is found in organs containing a large amount of extracellular tissue fluid, for which it presumably has some affinity. The biliary tract is the main channel for excretion of the dye but it is also retained in the kidneys of cats and rabbits.

The haematological actions of Congo red were studied by Richardson (1939, b). He found that Congo red in concentrations of 1 to 1,000 protects human erythrocytes against haemolysis by various solutions, apparently by virtue of its exerting a film effect on the red blood-cells. Thus Congo red prevented haemolysis in the presence of hypotonic saline, hypertonic urea, and sodium taurocholate solutions, but failed to do so in hypotonic dextrose solution and in ether and urea in aqueous solutions. Intravenous doses of 10 to 50 mg. per kg. body weight had no effect on rabbits' blood but 100 mg. produced a slight transient anaemia. One intravenous injection of more than 25 mg. per kg. caused a leucocytosis and marked increase in sedimentation-rate in rabbits. Only large doses produced anticoagulating effects.

in the blood, and smaller doses did not reduce the bleeding and clotting time. Richardson concluded that the use of Congo red clinically as a haemostatic was unsupported by experimental evidence, but he conceded that the action of the dye might be different in pathological states

Richardson, A. P (1939, a) *Amer. J. med. Sci.*, **198**, 82.

— (1939, b) *ibid.*, **198**, 87.

and Dillon, J. R (1939) *ibid.*, **198**, 73

Cysteine Hydrochloride

Anticoagulant Properties

T. J. Putnam and P. F. A. Hoefer investigated cysteine hydrochloride as an anticoagulant for clinical use. Coagulation may occur in normal vessels in polycythaemia, after operations, and in multiple sclerosis and certain forms of 'encephalitis' due to thrombosis of small cerebral vessels. Thrombosis may be due to increased or diminished coagulability of the blood plasma, increased or decreased powers of agglutination of the blood corpuscles, or slowing of the blood stream. Intracardial injections of cysteine hydrochloride were found to increase the clotting time 25 to 100 per cent in dogs. Six patients suffering from multiple sclerosis were given a 10 per cent solution of cysteine intravenously in physiological saline. 17 others were given 3 to 5 g daily by mouth, larger doses producing gastric symptoms. Untoward symptoms occurred in 3 patients, namely increased menstruation in 2 and skin ecchymosis in the other. The coagulation time rose from 30 to 90 per cent in these patients. A further 7 patients were treated in whom the coagulation time was not studied. The series was considered too small and the time too short for the clinical value of the drug to be determined. It was suggested that it might be used prophylactically to prevent post-operative thrombosis and in established thrombosis to prevent its extension.

Putnam, T. J., and Hoefer, P. F. A (1939) *Amer. J. med. Sci.*, **198**, 502

Ergot and Ergotamine Tartrate

Toxic Effects

M. W. Comfort and C. W. Frickson reviewed the literature on the untoward effects from the use of ergot and ergotamine tartrate. They quoted 2 cases from the literature in which gangrene developed after ergot had been given for puerperal sepsis. They themselves reported 2 cases in which ergotamine tartrate was given for puerperal sepsis. One resulted in gangrene of the right hand, and the other in cessation of radial pulsation which returned when the treatment was discontinued. These untoward effects seem to have no necessary relation to the dose, as patients may have an idiosyncrasy for very small ones. The earliest symptoms of ergotism are headache, nausea, vomiting, diarrhoea, tinnitus, and vertigo and they should be watched for during treatment. When they appear, the drug should be stopped and vasodilating drugs given, including alcohol by mouth.

Comfort, M. W., and Frickson, C. W (1939) *Ann. intern. Med.* **13**, 46

Eupaverin

Effects on Pulmonary Circulation

H. H. Bradshaw and R. J. Chodoff investigated the effects of eupaverin on the pulmonary circulation. The drug was found to have an immediate effect in lowering systemic blood-pressure. This effect was very transient, and was followed by a slight increase in blood-pressure. In the pulmonary circulation, however, the drug regularly caused a marked increase in blood-pressure over the original level. When eupaverin was given after oil emboli, the effects were qualitatively the same, increased pulmonary pressure and decreased systemic pressure. Some animals after receiving oil followed by eupaverin failed to survive. It is therefore difficult to understand how the drug could favourably influence the course of either pulmonary or systemic emboli. The drug has certain spasmolytic actions causing a marked, though transient, fall in systemic blood-pressure. Previous investigations have shown that

this is probably due to the action directly on the smooth muscle of the vessel wall. Eupaverin does not lower, but raises, the pulmonary arterial pressure in cats.

Bradshaw, H. H., and Chodoff, R. J. (1940) *Surg. Gynec. Obstet.*, **70**, 768

Heparin

Effect in Preventing Peritoneal Adhesions

F. P. Lehman and I. Boys investigated the prevention of peritoneal adhesions with heparin. Adhesions are formed from an exudate, serous or sero-purulent, on the peritoneal surface. Because heparin prevents the formation of fibrin in the blood it was used in an attempt to prevent the formation of these adhesions. Heparin was introduced into the peritoneal cavities of the dog and rabbit in which adhesions had been produced by contamination or by mechanical means. It proved to be very effective. Its chief danger is that it may lead to peritoneal haemorrhage. This only occurs if intraperitoneal haemostasis has not been secured before the abdomen is closed. The authors stated that more work must be done before a clinical trial is warranted. It may prove of use in preventing adhesions and possible obstruction in the abdomen, and in preventing adhesions in other serous cavities such as the joints.

Lehman, I. P., and Boys, I. (1940) *Ann. Surg.*, **111**, 427

Insulin

Pancreatrophic Principle

H. P. Marks and F. G. Young found that the daily administration of a crude anterior pituitary extract to normal rats for 2 weeks led to a rise of the insulin content of the pancreas to nearly twice its normal value. The 'insulin-increasing' or pancreatrophic substance, responsible for this rise, accompanied the diabetogenic and growth-promoting substances during ammonium sulphate fractionation of a crude extract, but it was not identical with either of these principles. The diabetogenic and growth-promoting substances also were not identical. Extracts which proved insulin-increasing in the rat might either reduce the insulin content of the dog pancreas to a low level or leave it without significant change, according to whether or not the extract was diabetogenic. The insulin-increasing action of a crude fresh extract of anterior lobe might be obscured in the dog by the diabetogenic action of the extract. From the evidence available it was assumed that the anterior lobe of the pituitary contained a 'pancreatrophic' or 'insulin-increasing' substance which was not identical with either the diabetogenic or growth-promoting principle, but at present it could not be assumed that the substance was a hormone.

Zinc-Protamine Insulin

Effects on non-diabetic individuals. D. Goldman investigated the effects of large doses of zinc-protamine insulin in non-diabetic schizophrenic subjects. It was found that such individuals tolerated huge doses, and most of the time remained free from hypoglycaemic symptoms in spite of low blood-sugar levels. Such levels were not necessarily of serious significance, nor were they hard to control. It was also found that prolonged high dosage of insulin did not disrupt the patients' endogenous insulin mechanism or sugar tolerance. Other noteworthy findings were marked fluctuation of blood-sugar levels during 24-hour periods, and marked transient gains in weight in most patients. The initial dosage was 15 units, and this was increased so that, in some cases, as much as 150 units were given twice daily; most patients tolerated over 100 units daily. The treatment was carried out for periods varying from 16 to 18 days. Improvement in the mental condition occurred in many of the patients, though some who improved only moderately on zinc-protamine insulin, responded brilliantly after being placed on regular insulin-shock treatment.

Goldman, D. (1940) *Endocrinology*, **26**, 612.

Marks, H. P., and Young, F. G. (1940) *Lancet*, **1**, 493

Nicotinic Acid

Effect on Peripheral Vascular System

R. J. Popkin administered nicotinic acid orally to determine its action on the

peripheral circulation. Its immediate effect was to produce a temporary flushing of the skin with tingling of the face and ears and slight vertigo. The blood-pressure was mostly unaffected. While the respiratory and pulse rates varied slightly, the differences in surface temperatures were considerable, even independently of the amount of the drug employed. When the oscillogram was used it showed a decrease in the amplitude of the tracings in 11 out of 13 cases. The author considered that some of the symptoms of nicotinic acid were produced by its histamine-like action, but held that such unpleasant symptoms made it practically valueless in the treatment of peripheral vascular disease; in addition, any favourable effect was purely temporary.

Popkin, R. J. (1939) *Amer. Heart J.*, **18**, 697

Posterior Pituitary Extract

Effect on Non-Gravid Uterus

A McLellan investigated the response of the non-gravid human uterus to posterior pituitary extract and its fractions oxytocin and vasopressin. Forty-three normal women were investigated. The cervix was dilated and a rubber bag filled with water introduced into the uterus. The movements of the uterus after injections were then recorded. It was found that the uterus responded to posterior pituitary extract before and during menstruation and in the early interval part of the cycle. Vasopressin caused contraction of the uterus, but oxytocin had no effect upon it.

McLellan, A. (1940) *Lancet*, **1**, 919

Potassium Iodide and Ipecacuanha

Relative Value as Expectorants

S. Alstead investigated the relative efficacy of potassium iodide and ipecacuanha as expectorants in 17 consecutive cases of chronic bronchitis. All the patients were adult males with typical physical signs. The diagnosis was, however, confirmed by X-ray examination. The patient collected his sputum in a graduated glass tube throughout the investigation; the amount of sputum was measured and recorded every 24 hours. For 3 to 4 days no drug treatment was given, then for a similar period a placebo, consisting of tincture of cochineal in water was given. Thereafter for about 7 days 5 to 10 grains of potassium iodide was added to each dose of the cochineal solution. Finally, for about 9 days, 50 minims of tincture of ipecacuanha and the iodide were added to each dose of the placebo. The drugs together did not produce a more copious or more fluid sputum. Only 4 of the patients produced more sputum when treated with potassium iodide. The cough and signs in the chest lessened in some of the patients, probably due to their treatment in hospital and rest in bed.

Alstead, S. (1939) *Lancet*, **2**, 932

Progesterone and Desoxycorticosterone Acetate

Absorption of Subcutaneously-Implanted Tablets

M. H. Warwick and A. S. Parkes investigated the absorption of progesterone from implanted tablets of substantial size, about 4 mm. in diameter and 1 to 3 mm. in thickness. Progesterone was absorbed from these tablets implanted subcutaneously at an average rate of about 20 per cent per month. Tablets weighing 50 mg. thus supplied about 10 mg. per month. The effect of acetylation of desoxycorticosterone on the rate at which the latter is absorbed from implanted tablets was also investigated. It was found that free desoxycorticosterone is absorbed more than twice as rapidly as desoxycorticosterone acetate.

Warwick, M. H., and Parkes, A. S. (1940) *Lancet*, **1**, 406

Saccharin

In War Time

The Académie de Médecine of Paris in response to the Minister of Health appointed a committee to consider the use of saccharin. The report presented by M. Lapique, which was approved by the Académie on April 9, stated that

saccharin was not toxic, even in amounts much larger than are likely to be taken, and recommended that in the present circumstances the dietary use of saccharin, except when combined with various other unnamed sweetening agents, be recommended. This confirms a decision reached in 1917, when the suggestion that it might exert an antidiastatic action and so cause indigestion was considered. The prolonged use of saccharin by many patients with diabetes mellitus without complaints and the absence of reports in the years 1917-1919 recording bad results further strengthened the conclusion. The supposed antidiastatic influence has been explained by its acid function which interferes with digestive ferments, such as the pancreatic, by raising the pH

M Lapicque (1940) *Bull Acad Méd Paris*, **123**, 287.

Secretin

Therapeutic Uses

L Camus and C Sacate describe cases in which secretin, which is extracted from the mucosa of the duodenum and jejunum and stimulates the pancreas, liver, and gall-bladder, was used, and quote the recorded therapeutic observations on the use of secretin in diabetes mellitus, diarrhoea, and dyspepsia. They injected intravenously 40 units of secretin in cholecystitis instead of instituting duodenal drainage, the resulting freedom from pain and hypersensitivity was very satisfactory. Some patients reacted with shock and other signs of intolerance and subsequently intramuscular and subcutaneous injections only were given. It was thought that the antispasmodic and regulating action of the secretin upon the duodenum might eventually establish a better co-operation between the pylorus and duodenum and the rest of the digestive tract. In cholecystitis and painful conditions of the gall-bladder intramuscular injections of secretin had a general sedative effect upon the gall-bladder and the whole digestive system. Sometimes a series of injections is necessary. In some forms of colitis associated with gall-bladder disease, the state of the faeces and their frequency improve. After injection of secretin there is a fall in the faecal organic acids, ammonia, and in the urinary indoxyl. In constipation associated with gall-bladder disease the bowels became more regular after injections of secretin. Migraine and headache disappeared after small intramuscular injections of secretin.

Camus, L., and Sacate, C. (1939) *Pr. med.*, **47**, 1368.

Sodium Diphenylhydantoinate

Anticonvulsant Properties

H. H. Goldstein and J. Weinberg, investigating the anticonvulsant properties of sodium diphenylhydantoinate, gave cardiazol (leptazol) to a group of 19 epileptic patients to increase seizures. This drug produced major epileptic seizures in 52.68 per cent. When sodium diphenylhydantoinate was given for a month or more previous to the administration of leptazol, the number of *grand mal* seizures fell to 7.14 per cent.

Toxic Effects and their Treatment

H. H. Merritt and T. J. Putnam investigated the regulation of the dose of sodium diphenylhydantoinate in the treatment of convulsive seizures, and also the treatment and prevention of the toxic effects of the drug. The amount of the drug which can be given with safety varies with each patient, and must be found by trial. In the authors' experience 3 to 9 grains daily would control fits and produce no toxic symptoms in various individuals. It is better to give the drug after or during a meal, and, if it is known when to expect a fit, the whole daily dose may be given before that time in order to get a high concentration in the blood and prevent the fit. Nocturnal fits have been successfully treated in this way. Toxic effects include nausea, vomiting, mental changes, dermatitis, and hypertrophy of the gums. The drug has no significant effect upon the haemopoietic system. The toxic effects would therefore appear to be different from those of the barbiturates and bromides. Merritt and Putnam believe that the drug is not so likely to produce dangerous

results as barbiturates and bromides sometimes do, and should therefore be used for patients whose fits cannot be controlled by more usual methods of treatment.

Goldstein, H. H., and Weinberg, J. (1940) *Arch. Neurol. Psychiat.*, Chicago, **43**, 453

Merritt, H. H., and Putnam, T. J. (1939) *Arch. Neurol. Psychiat.*, Chicago, **42**, 1053

Strophanthin

W. A. Brams *et al.*, investigating the toxicity and clinical value of strophanthin, found that single intravenous injections of 0.5 to 0.75 mg. of strophanthin K. in normal individuals failed to produce significant clinical or electrocardiographic evidence of toxicity. The use of 0.3 to 0.5 mg. in patients with severe cardiac failure, most of whom also had hypertension and regular rhythm, also gave rise to no toxic effects. The continued injection of 0.3 mg. daily for as long as 24 days failed to produce evidence of toxicity in patients with cardiac failure. The therapeutic results obtained with strophanthin appeared to be comparable in every way with those obtained by adequate digitalization, when digitalis was given orally. The authors did not advocate strophanthin, in place of digitalis, in the routine management of cardiac failure. Its speed of action, however, rendered it ideal in acute cardiac emergencies, in marked congestive failure in which oral digitalis was absorbed with some uncertainty, and in cases where digitalis was ineffective.

Brams, W. A., Golden, J. S., Sanders, A., and Kaplan, I. (1939) *Ann. intern. Med.*, **13**, 618

Sucrose and Other Solutions

Diuretic Effect

H. F. Helmholz and J. L. Bollman experimented with rabbits to ascertain the diuretic effect of certain solutions. They found that 130 c.cm. per kilogram body weight of a 20 per cent solution of sucrose could be injected in 1 hour in a rabbit without lethal effect. It produced urinary excretion up to 136 per cent of the volume of fluid injected. More than 90 c.cm. of a 20 per cent solution of glucose per kilogram body weight in 1 hour was fatal, but the injection of slightly less produced a diuresis of 73 per cent of the volume of fluid injected. Sucrose produced no permanent damage in the kidneys of the animals injected. Solutions of sodium sulphate, urea, glucose, and sorbitol equivalent in toxicity to 20 per cent glucose solution were similarly injected and they all produced less diuresis. All these solutions except sorbitol were more toxic than sucrose and several of the animals died after their first injection of one of them. Attempts to produce and maintain an intense diuresis with continuous intravenous injection of sucrose or Ringer's solution for 6 hours ended mainly in failure. Most of the animals died before the end of the 6-hour period. In order to prevent toxic effects and death it was found necessary to maintain a balance between the solution injected and the urine excreted with reference to water, sucrose, and salt. Eight per cent sucrose in Ringer's solution of half strength promoted a diuresis of slightly more than half the body weight of the animals during the 6 hours. Helmholz and Bollman concluded that isotonic solutions of different substances do not produce the same amount of diuresis, therefore these diuretics must have some specific action upon the kidney apart from the withdrawal of water by osmosis.

Intravenous Hypertonic Sucrose Solution

Renal changes.—W. A. D. Anderson and W. R. Bethea found distinctive renal lesions in 6 cases following the intravenous administration of hypertonic solutions of sucrose. The lesion is characterized primarily by extreme foamy swelling of the lining cells of the renal convoluted tubules. The change may progress to death of the cells. The authors concluded that the administration of hypertonic solutions of sucrose to patients with renal damage is inadvisable. Large or repeated intravenous doses of sucrose should be avoided.

Anderson, W. A. D., and Bethea, W. R. (1940) *J. Amer. med. Ass.*, **114**, 1983.

Helmholz, H. F., and Bollman, J. L. (1939) *Proc. Mayo Clin.*, **14**, 567.

Sulphonamide Compounds

Dosage for Children

M Hynes studied the effects of different doses of sulphonamide drugs on the blood of 81 children. The optimal concentration of the drugs in the blood is 4 to 10 mg per 100 c.c.m. The estimations were made 24 hours or more after beginning treatment. The results suggested that there was a rough correlation between the dose of sulphapyridine, its concentration in the blood, and the weight of the patient. Similar results were obtained with sulphanilamide and proseptasine. The following dosage table is suggested.

Age	Dose (0.5 g. tablets)	Dose per 24 hours in grams
0-3 months	1, 4 hourly	0.75
3-6 "	1, 6 hourly	1.0
6-18 "	1, 4 hourly	1.5
1½-4 years	1, 6 hourly	2.0
4-8 "	1, 4 hourly	3.0
8-12 "	2, 6 hourly	4.0
Adult	2, 4 hourly	6.0

However, rates of absorption and excretion are so variable that certain results can only be guaranteed by blood estimation in each individual case.

Toxic Effects

W. S. Tillett reviews the toxic effects of the sulphonamide compounds, especially sulphapyridine. It is now clear that sulphanilamide and to a great degree sulphapyridine undergo chemical changes in the body, one being acetylation. This particular chemical change results in the formation of a poorly soluble compound which readily crystallizes out of solution, and mechanically rather than chemically damages the cells of the body. This damage may exert a delayed effect over months and years and especially so in the urinary tract and the bone-marrow. The crystals may damage the lining epithelium of the renal tubules, pelvis and ureters, and cause haematuria, and in time by accumulation lead to the formation of calculi with renal colic, and mechanically to dilatation of the renal pelvis, damming back of urine, pyelonephritis and pyelitis, and finally nephritis with nitrogen retention and renal insufficiency. The earliest reports on the treatment of patients by sulphapyridine did not mention haematuria, but recent accounts have shown successive increases in its percentage incidence from 2 to 18 and 25; it occurs in both children and adults, and sometimes in alkaline as well as in acid urine. Of much more importance than the transient and almost uniformly harmless toxic effects on the nervous system and the very common nausea and vomiting, especially after sulphapyridine are those on the haemopoietic system. Most of the fatalities due to sulphonamide treatment are due to this cause: 6 deaths have been directly attributable to the action of sulphapyridine, and rather more have been caused by sulphanilamide, but the numbers are small. The granulocytes suffer more than the lymphocytes, and in fatal cases the leucocyte bone-marrow is damaged in an irreversible manner, even if the administration of the drug is stopped. When the erythrocytes are mainly affected, there may be an acute haemolytic anaemia, or a secondary anaemia, down to half the normal count, but this passes off when the administration is discontinued. It seems probable that the leucocyte changes occur in the bone-marrow, and that the mature red cells in the circulation are the most vulnerable to haemolysis. The author calls attention to the problem of the combined action of sulphonamides and other reagents of chemical or biological origin in increasing, supplementing, altering or inactivating effects on the body.

I. H. Bensley also discussed the toxic effects of sulphonamide drugs on the basis of 420 cases, of which 305 were treated with sulphanilamide and 115 with sulphapyridine. In this series of cases no deaths occurred due to either of the drugs. In 8 cases major toxic effects were encountered, these were agranulocytosis in 2 cases treated with sulphanilamide, severe methaemoglobinuria in 2 cases treated with sulphanilamide, and severe renal disturbance in 2 cases treated with sulphapyridine. The following precautions were observed in the use of these drugs. Frequent estimations of the concentration of the drug in the blood were made, concentrations higher than 15 mg per 100 c.c.m. being avoided. When drug fever occurred the

drug was discontinued, except in cases in which the life of the patient depended on continuance of the drug. Administration of the drug over a period of 2 weeks or more was avoided unless the nature of the infection obviously justified prolonged treatment. Frequent spectroscopic examinations of the blood were made for methaemoglobin and sulphaemoglobin. Methaemoglobinaemia was found in 114 cases, but in most cases it was mild. When severe it was readily overcome by reducing the dose, except in 2 cases, both of these were successfully treated by blood transfusions, and one also by the intravenous injection of methylene blue. Mild sulphaemoglobinaemia was found in 3 cases only. Other precautions taken were red-cell counts, plasma-bilirubin estimations, and white-cell counts. The severe renal complication which occurred in 4 cases receiving sulphapyridine was characterized by gross haematuria, variable amounts of pus, oliguria, oedema, nitrogen retention, and abdominal pain of the nature of that in renal colic. In 2 of these cases these manifestations disappeared within a few days of discontinuing the drug. In the other 2 they were more persistent, in one case being still present 16 weeks later when the patient was discharged from hospital. There was no evidence of calculus formation. The authors concluded that, provided the precautions described above are observed, sulphanilamide therapy is relatively safer, on the other hand, because of the possibility that sulphapyridine may lead to severe and perhaps permanent renal damage, this drug must be regarded as potentially dangerous, even when all the known precautions are observed.

Cyanosis.—D. Campbell and T. N. Morgan stated that cyanosis produced by the administration of sulphonamide compounds is always due to the presence of either sulphaemoglobin or methaemoglobin and one or other of these substances will be found in the blood if a careful spectroscopic examination is made. When looking for methaemoglobin it is essential that the blood should be laked with only a small quantity of water (not more than 1 in 5) so that the pigment is in a concentrated solution, and that the blood should be examined as soon after withdrawal as possible. They found that methylene blue given either intravenously, intramuscularly, or orally will convert methaemoglobin into haemoglobin and cause the cyanosis to disappear. They reported 2 cases receiving 2-(*p*-aminobenzene)sulphonamido-pyridine (sulphapyridine) who were relieved of their cyanosis due to methaemoglobin in from 5 to 10 minutes by the intravenous injection of from 150 to 350 mg. of methylene blue. In 2 other cases the cyanosis disappeared after giving 360 to 400 mg. of methylene blue intramuscularly. If the cyanosis returned the treatment was continued and methylene blue given daily by mouth in 1 g. doses. Methylene blue was found to have no effect on cyanosis due to sulphaemoglobinaemia.

Effect on kidneys.—I. Snapper *et al.* reported a few cases in which the administration of sulphonamide compounds produced changes in the kidney. In a few patients haematuria occurred and in some calculi developed in the urinary passages, one of these cases was fatal. Chemical investigation of the calculi proved them to be crystals of acetylsulphapyridine, which had been precipitated in the renal pelvis.

Effect on Human Tubercle Bacillus

R. H. Follis investigated the effect *in vitro* of sulphanilamide, acetylsulphanilamide and sulphapyridine on the human tubercle bacillus. It was found that, whereas sulphapyridine in concentrations of 50 mg. per cent, or even higher, exerts a special inhibitory effect on the growth of the bacillus, sulphanilamide and acetylsulphanilamide have little or no bacteriostatic effect.

Bacteriostatic and Germicidal Effect in Urine

J. H. Hill, investigating the *in vitro* action of sulphanilamide, sulphapyridine, and sulphathiazole in the urine, found that, at the 50 and 100 mg. per cent levels, there was little difference between the drugs. When large numbers of bacteria were employed, such as are often found in urinary infections, no germicidal action was obtained. When the numbers were reduced to thousands, marked bacteriostatic or germicidal action was obtained with the three drugs. All of the drugs were more effective in acid than in alkaline urine. The much larger amounts of sulphathiazole which may be expected in urine, as compared with sulphanilamide and sulphapyridine, indicates that sulphathiazole will prove to be a more valuable urinary antiseptic than either sulphanilamide or sulphapyridine.

Effect on Haemoglobin Metabolism and Hepatic Function

C. J. Watson and W. W. Spink found that, in the ordinary therapeutic doses, sulphanilamide causes acceleration of the metabolism of haemoglobin, characterized by an increase in urobilinogen in the faeces and a varying increase in the reticulocyte percentage. The most marked acceleration of haemoglobin metabolism is represented by the unusual cases in which marked haemolytic anaemia occurs. Sulphapyridine appears to have the same effect as sulphanilamide in haemoglobin metabolism. The occurrence of macrocytic or normocytic mildly hypochromic anaemia after administration of sulphanilamide or sulphapyridine indicates disturbance in haemoglobin formation in addition to increased haemolysis.

Sulphanilamide

Lactation in breast milk. Lucile R. Haas *et al.* investigated whether the prolonged use of sulphanilamide at therapeutic blood-levels resulted in an accumulation of the drug in breast milk sufficient to harm the infant receiving it. Twenty-five lactating women were given sulphanilamide in therapeutic doses for 3 days. It was excreted as free sulphanilamide and acetylsulphanilamide in the milk. The level in the milk was always higher than that in the blood. The excretion was low on the first day, rose slightly on the second and third days, and was highest of all on the fourth and fifth days when the drug had been stopped. These levels were also true for the blood and the urine. The total amount excreted in the milk over a period of 5 days was never greater than 0.23 g., 1.6 per cent of the total dose ingested. This was so small that the authors concluded that it would not harm the infant unless the latter were especially susceptible.

Placental transmission.—H. Speert investigated in rats the placental transmission of sulphanilamide and its effect upon the new-born. The drug is often given to pregnant women and, although one dose has been found not to injure the infant, the effects of prolonged dosage on the foetus are more uncertain. Speert found that the prolonged use of the drug had a harmful effect upon the foetus of the rat. Postnatal and antenatal mortality were increased. The young rats were smaller and their growth was stunted. The litters were also smaller in size. The blood concentration of sulphanilamide was equal in the mother and the foetus. It therefore was reasonable to attribute the harmful effects to the presence of the drug. The toxic effects may partly be due to the formation of acetylsulphanilamide in the blood of the rat. Although in this series relatively larger amounts of sulphanilamide were given than is usual to pregnant women, Speert concluded that the drug should be used with great care in this condition.

Influence of proteolytic products on effectiveness. J. S. Lockwood and Helen M. Lynch studied the influence of proteolytic products on the effectiveness of sulphanilamide. They found that addition of peptone to the media inhibited the action of sulphanilamide because of the excess of nitrogen produced. Haemolytic streptococci, staphylococci, pneumococci, and *Bact. coli* were investigated. The concentration of the sulphanilamide as well as the presence of the peptone influenced the action of the drug. The fact that sulphanilamide becomes powerless in the presence of added peptone suggests that its bacteriostatic action is due to its preventing in some way the organism from combining with nitrogenous products. This hypothesis would account for the fact that the drug is only effective in conditions such as pneumonia when a lot of tissue is not destroyed and therefore nitrogenous products are not present in large amounts. It similarly accounts for the failure of sulphanilamide in the treatment of large abscesses when there is much tissue proteolysis.

Bacteriostatic effect in vitro.—T. C. Stamp investigated the bacteriostatic action of sulphanilamide *in vitro*. He found that a fraction isolated from a broth culture of a group C haemolytic streptococcus was capable of antagonizing this bacteriostatic action, and that of sulphapyridine *in vitro*. This fraction contains free amino-acids and is protein free. A similar fraction was isolated from a group A haemolytic streptococcus. It was extracted by means of dilute NH_4OH and is resistant to heat, dilute acids, and alkalis. It appears to be non-specific in action. It was suggested that these drugs exert an inhibitory influence on certain enzymes concerned in bacteriostatic action. To explain the antibacteriostatic action of these fractions Stamp suggested that the fraction may contain a necessary nutritive

factor, the production of which is interfered with by the drug, or that the fraction is an essential part of the enzyme system affected by the drugs.

Effect of pH on bactericidal power of urine containing sulphanilamide—J. R. Sickler investigated the effect of the pH on the bactericidal power of urine containing sulphanilamide. Specimens of urine taken 24-hourly from normal men taking sulphanilamide by mouth were pooled and collected. The specimens were sterilized by passage through a Berkefeld filter, and the amount of free sulphanilamide in them determined. The specimens were then adjusted to the desired pH by the addition of acid or alkali and incubated with various organisms isolated from the infected human urinary tract. Experiments with *Bact. coli communis* showed that, as the concentration of sulphanilamide increased in the urine, its bactericidal power increased, and it was also increased by making the urine more alkaline. *B. proteus* and *Staph. aureus* were also killed in larger numbers by the more alkaline urine. The pH of this urine was 7.7. In order to show that it was not the alkalinity alone which produced the result, tests were made with alkaline urine containing no sulphanilamide. It was only when the pH reached 9.5 that this urine showed any increase in bactericidal power. Even under intense alkaline therapy human urine probably never rises above pH 8.0.

Presence in aqueous and vitreous—W. G. Mengel investigated the amount of sulphanilamide present in the aqueous and vitreous after conjunctival and oral administration. The experiments were made on blind eyes, blind from absolute glaucoma or phthisis bulbi. An 0.8 per cent aqueous solution of sulphanilamide was dropped into the eye, 3 drops every 15 minutes for 6 times, then 3 drops every 5 minutes for 6 times. For comparison 2 doses of 15 grains each were given by mouth 6 hours apart and the aqueous was examined $4\frac{1}{2}$ hours later. After an interval of 5 days, 15 grains every 2 hours for 3 doses was given orally before the examination of the vitreous 2 hours later. Sulphanilamide was found in the aqueous after instillation into the conjunctival sac, but not in so great a concentration as when it was given by mouth. The concentration of sulphanilamide 32 minutes after oral administration was 1.1 mg. per 100 c.c. in the vitreous.

Second attack of drug fever—J. R. Gallagher reported the case of a boy of 18 years who was treated with sulphanilamide for a *beta*-haemolytic streptococcal throat infection. He was given 20 gr. of sulphanilamide 5 times daily and on the twelfth day developed a sulphanilamide drug fever, characterized by malaise and a diffuse morbilliform rash. Two years later he developed an acute urethritis and was given four 20-grain doses of sulphanilamide. He again developed the drug fever and Gallagher concluded that the first course of the drug sensitized the patient to it, so that only a small dose was necessary to bring on the fever on the second occasion. Gallagher stressed the importance of this observation, as the possibility of sensitizing patients to sulphanilamide should be borne in mind when prescribing it for minor ailments, as it may make it impossible to give it for any possible major illness later on.

Sulphapyridine

Excretion—G. V. James investigated the excretion of sulphapyridine in 2 women with puerperal fever and one normal man. Before the drug was given the blood and urine were tested and found to be negative for sulphonamide compounds. On continuous dosage of the drug for some days, about 90 per cent of it could be recovered from both the urine and faeces, by far the larger amount appearing in the urine. The excretion continued for some days after the drug had been stopped. When intravenous or oral administration resulted in vomiting, the drug could be recovered from the vomit. This shows that during intravenous administration the drug is excreted into the alimentary canal. No oxidation products similar to those found in sulphanilamide excretion were recovered, presumably because sulphapyridine is more difficult to oxidize.

Excretion in saliva—B. W. Fickling *et al.* investigated the cause of sulphapyridine appearing in the saliva during treatment with the drug. In 18 cases receiving the therapy, one by intravenous injection only, sulphapyridine was found in various concentrations in the saliva. To prove that its presence was not due to mechanical lodging of particles in the mouth two experiments were carried out. To a young healthy adult were given 2 tablets (1 g.) of the drug which were rolled around the

mouth for 2 minutes without swallowing and the contents of the mouth were then voided. Another chewed the tablets for 2 minutes and again without swallowing voided the contents. During the experiment saliva was not swallowed, but collected and examined each hour. Except for the half-hour after the beginning of the experiment in the first case, no sulphapyridine appeared in the saliva. On the other hand, if the drug were swallowed without chewing and the mouth then rinsed out, sulphapyridine appeared in the saliva within an hour of ingestion.

Advantages of hypodermoclysis - G. V. Taplin *et al.* employed sodium sulphapyridine by hypodermoclysis in more than 50 cases of pneumonia and other conditions in which sulphapyridine was indicated, but in which oral administration was difficult or impossible. The initial dosage employed was 3 to 7 g. dissolved in 1 litre of physiological saline solution. Subsequent doses were given at intervals of from 24 to 36 hours, the amounts depending on the response of the patient, the blood-level attained, and the reactions. The solution is given in the routine manner into the thighs or under the breasts, the average patient generally tolerating 200 to 300 c.c. per hour. No local reactions were observed in any case. Advantages of this method over oral administration are the absorption of the drug when vomiting precludes the oral route, and that a concentration in the blood of 4 to 10 mg. per 100 c.c. can be reached in a few hours, and maintained for from 18 to 36 hours. The sodium chloride requirement is met at the same time. The fluid intake is supplemented. Advantages over intravenous administration are that there is no danger of local reactions, which may occur if the solution escapes from a vein, and the effective concentration in the blood is maintained for longer 24 hours as compared with 12. The technique of administration is simpler.

Sulphanilamide and Sulphapyridine

Relative toxicity - W. H. Brown *et al.* investigated the relative toxicities of sulphanilamide and sulphapyridine. They found that the vomiting due to sulphapyridine appears to be of both local and central origin. Serious toxic manifestations were twice as frequent with sulphapyridine as with sulphanilamide. Oliguria, haematuria, pain in the costo-vertebral angle, and anuria are fairly common complications of sulphapyridine, especially when the blood concentration is high. These sequelae are related to the insolubility of acetylsulphapyridine, which precipitates in characteristic crystals in acid and alkaline urines. Leucopenia occurs with both drugs, but is more frequent with sulphapyridine. Acute haemolytic anaemia is more frequent with sulphanilamide. The authors concluded that sulphapyridine is more essentially toxic than sulphanilamide.

Sulphathiazole

Toxic effects - I. G. Reinhold *et al.* investigated the pharmacology and toxicity of sulphathiazole, 2-(*p*-aminobenzene-sulphonamido) thiazole in 83 patients with pneumonia, and in 9 convalescent patients who served as controls. They found that the drug was rapidly absorbed from the gastro-intestinal tract, and rapidly excreted in the urine. After the intravenous injection of the sodium salt, recovery of the drug in the urine was practically quantitative. It was not absorbed from the rectum. In most individuals the proportion of the drug conjugated is low. Kidney function was temporarily impaired to a varying degree in nearly all the cases. In 10 per cent of the patients, vomiting occurred, but was never sufficiently severe to interfere with the use of the drug. The incidence of other toxic reactions was small, microscopic haematuria occurred in 5, dermatitis in 3, and psychosis in 3, the latter explainable by the presence of chronic alcoholism. In case of absorption and excretion sulphathiazole resembled sulphanilamide. Because the former is more readily absorbed from the gastro-intestinal tract, and excreted more rapidly, its use is more easily controllable. In many ways it appears to be less toxic than sulphanilamide.

Skin, conjunctival and scleral reactions - J. W. Haviland and P. H. Long report 10 cases of skin reactions during sulphathiazole therapy. There were 3 types of rash: 3 were maculo-papular, 5 were urticarial, and 2 resembled erythema nodosum. In the urticarial type the skin of the extremities was primarily involved, although the rash in some cases spread to the trunk. An entirely new drug reaction also occurred in 6 of these cases. This was a conjunctival and scleral injection,

restricted mostly to the exposed portions of the bulbar conjunctiva and sclera. This was accompanied by a considerable amount of burning and a watery discharge from the affected eye. No similar lesion has been described after the use of any other sulphonamide derivative.

Concretions in renal tubules. D. S. Pepper and H. M. Horack found at necropsy of a patient treated by sulphathiazole, that the renal tubules were obstructed by concretions. On analysis the concretions were found to be a derivative of the drug. The gross and histological findings in the kidney were identical with those described by other authors as occurring in experimental animals. Because of the intrarenal precipitation of sulphathiazole it was considered that renal complications resulting from its use might be more serious than those following the use of sulphapyridine.

Sulphathiazole and Sulphamethylthiazole

Properties. R. L. Mayer reports the results of his experimental research for nearly 2 years on the properties of sulphathiazole and sulphamethylthiazole. These drugs, which are of low toxicity but wide potency, were tested both *in vitro* and *in vivo*. *In vitro* these thiazole compounds were found to exert a bacteriostatic effect on *β* haemolytic streptococci, pneumococci, *Staphylococcus aureus*, *Bact. coli*, and *Cl. tetani*, which is much more powerful than that of sulphapyridine and sulphanilamide. Tetanus toxin was neutralized much more effectively than by means of sulphapyridine. A large number of mice were used in the experiments on the *in vivo* action of the 2 thiazole compounds which were usually given in food immediately before the mice were infected with the bacteria. The conclusion reached was that the effects of the new preparations approach, may even equal, but never surpass those of sulphapyridine.

In *Staphylococcus aureus* infections. Sulphathiazole, which contains the parent sulphonamide radical and the thiazole radical, and its methyl derivative sulphamethylthiazole are both effective against infections by *Staphylococcus aureus* but, as W. E. Herrell and A. I. Brown point out, the methyl derivative is more powerful than sulphathiazole, which is also bacteriostatic to streptococci and pneumococci. These authors in a preliminary report bring forward laboratory experiments on cultures of *Staphylococcus aureus* grown in combination with (a) sulphanilamide, (b) sulphapyridine, (c) sulphathiazole, and (d) sulphamethylthiazole, these showed the great superiority as an antistaphylococcal drug of the sulphamethylthiazole. The same result was shown by experiments on mice infected with *Staphylococcus aureus*, and by 3 clinical cases of this infection. The dosage given of sulphamethylthiazole was 2 g. for 2 initial doses at intervals of 4 hours, followed by 1 g. every 4 hours.

Sulphamethylthiazole and Sulphapyridine

In experimental staphylococcal infections. A. Macdonald assessed the value of sulphamethylthiazole in mice experimentally infected with staphylococci. Sulphapyridine was also used. Neither drug had any effect on the lesions when given by mouth. Given intravenously, about half the mice survived 21 days when they had received staphylococci either intravenously or intraperitoneally. Sulphamethylthiazole was slightly more efficient in this respect than sulphapyridine. Many of the surviving mice were still infected with organisms and some of them had kidney abscesses. These results conform well with those of other workers on the sulphanilamide compounds.

Prontosil Soluble

Results of local application. J. A. Smith successfully treated a variety of conditions, such as a varicose ulcer, an abscess, and a septic burn by the local application of prontosil soluble. This method has the advantage that it is economical and avoids toxic reactions. The exact action of prontosil applied locally is unknown. It has, however, a powerful antibacterial effect and acts as a deodorant and a stimulant to healing.

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Tea Drinking

Effects

G. W. Halpenny and H. F. MacDermot, investigating the effects of tea drinking, found that good tea, brewed for 5 minutes, produces mild and pleasant stimulation, in no way corresponding with the violent, unpleasant action of its chief constituents, caffeine and tannin, when these are given separately or in combination. When brewed for 10 minutes, tea may produce some mild discomfort, but this is nullified by the addition of milk. Cheap tea has no objective effects, but, in strong infusion, may be unpleasant. The effects of tea on gastric acidity and on peptic activity are slight and variable. Tea does not increase gastric acidity, nor does it appear to alter the basal metabolic rate.

Halpenny, G. W., and MacDermot, H. L. (1939) *Canad. med. Ass. J.*, **41**, 449

Trasentin

Antispasmodic Effect in Gastro-Intestinal Disorders

I. Spier *et al.* employed a new synthetic drug, diphenylacetyldiethylaminoethanol (trasentin) in 32 patients. They found that the drug exerted a powerful relaxing effect on the gall bladder, and assumed that it had a similar relaxing effect on the bile ducts and on the sphincter of Oddi. The small intestine is also effectively relaxed by the drug. They found it helpful in several cases of duodenal and marginal ulcer, of gastritis, cholelithiasis, biliary dyskinesia, and spastic colon in which the usual therapy was ineffective. It stopped post-operative diarrhoea in 5 patients. The optimal dosage was 150 mg. by mouth, given 30 minutes before meals, or 75 mg. subcutaneously. Dryness of the mouth was observed in 2 cases. The authors concluded that the drug is a useful antispasmodic, and may prove invaluable in the treatment of diarrhoea, in intestinal fistula, and after operations which shorten the small intestine and upset its normal gradients.

Spier, I., Neuwelt, I., and Necheles, H. (1939) *Brit. med. J.*, **6**, 387.

Veritol

Effect on Blood-Pressure

G. Schoenewald *et al.* investigated the action of veritol (β -(*p*-oxyphenyl)-isopropylmethylamine), an isomer of ephedrine, on the blood-pressure of cats under various types and depths of anaesthesia. The rise of arterial blood-pressure under ether, chloralose, or pentothal varied in extent and duration. There was no direct relation between the blood-pressure response and the dose of veritol or the depth of anaesthesia. The blood-pressure response did not depend on its initial level. There was no difference in the results obtained in atropinized and non-atropinized cats. Veritol had a tachyphylactic action in cats; the second injection might cause a fall in blood-pressure. The drug had no pressor action in cats under chloroform, and only a negligible pressor action in cats under cyclopropane anaesthesia. Intravenous injection of veritol caused slight disturbances of cardiac rhythm in cats under ether; severe disturbances of rhythm were recorded electrocardiographically in cats under pentothal, chloralose, cyclopropane, or chloroform anaesthesia. These changes were also observed in atropinized animals.

H. Dodd and G. Merton found veritol (β -(*p*-oxyphenyl)-isopropylmethylamine) to be a reliable and satisfactory drug for restoring the blood-pressure during and after operations. Even when given intramuscularly, its action was rapid and certain, lasted half an hour or more, and produced no injurious effects. The rise in pulse rate, when present, was never excessive. The optimal dose was found to be 1 c.c., given intramuscularly, but 1.5 c.c. was not too great in a shocked or exhausted patient. For healthy patients whose blood-pressures are temporarily low, as after a moderate spinal anaesthetic, doses of 0.75 c.c. are indicated. Doses of less than 0.75 c.c. are not generally effective in an adult, unless given intravenously; given thus 0.75 c.c. is generally too much, and 0.25 c.c. is adequate. In an average patient, whose systolic blood-pressure has not fallen below 80 mm., an intramuscular injection of 1 c.c. will raise the blood-pressure to within about 20 per cent of the patient's normal systolic pressure; the action begins in from one to 5 minutes, reaches a maximum in about 18 minutes, and falls gradually over the next 30 minutes.

Dodd, H. and Merton, G. (1939) *Brit. J. Surg.* **27**, 78.

Schoenewald, G., Schweitzer, A., and Steel, G. C. (1940) *Lancet*, **1**, 544.

PHARYNX DISEASES

See also B.E.M.P., Vol. IX, p. 570, and Surveys and Abstracts 1939, p. 90.

Acute Pharyngitis

Streptococcal

Sulphonamide therapy. P. S. Rhoads and M. L. Afremow treated with sulphanilamide 31 cases of sore throat due to the haemolytic streptococcus. Thirty-six control cases were also studied. All the patients had fever, and many had exudates on the throat. Both groups were treated with rest in bed, hot alkaline gargles, and either codeine or acetylsalicylic acid for body pains. The average daily dose of sulphanilamide in the treated group was 54 grams, and the treatment lasted for an average of 5.6 days. Toxic manifestations occurred in 16 of the patients. Nausea and vomiting were the most frequent, but precordial pain and hallucinations occurred. When the drug was discontinued the reactions subsided. The drug had no influence on the illness, nor altered the incidence and type of complications in this series when compared with the controls. Nor did it have any effect on the duration of the carrier state. Rhoads and Afremow concluded that although the drug appears to have no effect on this superficial infection it should not be withheld if deeper infectious states such as otitis media supervene.

Rhoads, P. S., and Afremow, M. L. (1940) *J. Amer. med. Ass.*, **114**, 942.

Chronic Pharyngitis

Associated with the Plummer-Vinson syndrome.—D. P. Cordray believes that in

the true Plummer-Vinson syndrome a 'web' is the cause of the anaemia, since it forms a barrier to adequate nutrition. The outstanding pathological change in mice fed so as to maintain severe anaemia for several months, was hyper-keratinization of the epithelial layer and increase in the usual number of mitotic figures. This combination is considered by many pathologists as a precancerous lesion. Since the only possible aetiological factor is the secondary anaemia, it is reasonable to infer that marked, protracted secondary anaemia can produce precancerous lesions in the oesophagus.

Cordray, D. P. (1940) *Ann. Otol., etc., St. Louis*, **49**, 160.

PHLEBOTOMUS FEVER

See also B. L. M. P., Vol. IX, p. 583.

Harara (*Urticaria Multiformis Endemica*)

F. Jacobsohn showed a man, aged 47, whose arms and legs (extensor and volar aspects) presented a condition resembling lichen urticatus. Some of the lesions were impetiginized, and on the soles of the feet there were serous and haemorrhagic blisters. The condition began in Palestine where it is endemic during the months May to November, chiefly in immigrants and children, it is due to the bites of the sand-fly, and may last 3 to 4 months.

Jacobsohn, F. (1939) *Proc. R. Soc. Med.*, **32**, 1586.

PINK DISEASE

See also B. L. M. P., Vol. IX, p. 603, Cumulative Supplement, Key No. 1261, and Surveys and Abstracts 1939, p. 475.

Treatment

Vitamin B₁

G. Forsyth, in view of the resemblance of pink disease in children to beri-beri and pellagra, treated 4 cases with vitamin B₁ in large doses. Following the oral administration of 600 units daily, a rapid improvement in symptoms generally occurred within a few days and in several cases the condition cleared up within 2 weeks. The author thinks that the condition is either a deficiency disease or due to a virus which particularly attacks the peripheral nervous system.

Forsyth, G. (1939) *Med. J. Aust.*, **2**, 751.

PITUITARY GLAND DISEASES

See also B. E. M. P., Vol. IX, p. 611, and Surveys and Abstracts 1939, pp. 108 and 476.

Anatomy and Physiology

Hypothalamic-Pituitary Syndromes

L. Lichtwitz in discussing the hypothalamic-pituitary syndromes first refers to Claude Bernard's conception of a constant internal environment and then to Joseph Barcroft's dictum that 'the physiology of the hypothalamus is the physiology of the internal environment'. The hypothalamus responds to many stimuli, such as temperature, osmotic pressure, and pH, and is itself influenced by hormones, for example, the main action of thyroxine has been stated to be exerted on the hypothalamus, and in all probability the inhibitory influence of a number of endocrine glands on the anterior pituitary is effected through the hypothalamus. The pituitary-hypothalamic complex is responsible for many symptoms, syndromes, and well-defined diseases. The secretion of the anterior pituitary is controlled by the hypothalamus, and it is therefore practically impossible to determine which function or lesion is purely pituitary or purely hypothalamic in origin. The functions depending on hypothalamic-pituitary activity are general metabolism; carbohydrate metabolism, fat metabolism and distribution of fat; water metabolism (renal activity

and sweating); thirst; hunger and appetite, growth and trophism, sexual development, maturation, and activity, cardiovascular activity (cardiac rhythm, blood-pressure, vasomotor balance, and circulating blood volume), gastro-intestinal activity (secretions, tonus, peristalsis), formation of erythrocytes, leucocytes, thrombocytes, and plasma proteins, regulation of body temperature, and sleep (hypothalamic only). The disorders of these functions are numerous and show plus-minus forms, for example, high and low basal metabolic rates, diabetes mellitus and hypoglycaemia, gigantism and dwarfism, insomnia and somnolence, precocious puberty and delayed sexual development. The hypothalamus is an essential instrument for emotional expression which is normally under the control of the cerebral cortex, and when in hypothalamic disorders the cortical control is weakened or lost, emotional instability and abnormal behaviour become prominent. The occurrence of hypothalamic emotional attacks has so far not been fully recognized. The hypothalamic-pituitary syndromes are due to 4 main causes: (i) inherited or congenital defects, heredity plays an important part in diabetes insipidus and Frohlich's dystrophia adiposo-genitalis; (ii) inflammation, encephalitis due to all infective diseases, not to influenza only, (iii) injury, such as operation, (iv) tumours, primary or metastatic, leukaemic infiltration, Boeck's sarcoid, lymphogranulomatosis, and xanthomatosis may also be responsible. Accounts are given of diabetes insipidus, infantile gigantism, and adiposogenital dystrophy. Three types of diabetes insipidus are described: (i) polyuria only, (ii) polyuria with failure to concentrate chlorides, bicarbonates, and basic elements, (iii) with very slight, if any, polyuria but with the failure to concentrate. E. P. Pick of Vienna established the antidiuretic effect of antipyretics, amidopyrine being specially effective on the nocturia of chronic mesencephalitis. In present Germany infantile gigantism is portrayed as the ideal of manhood and knighthood in the statue of Siegfried. Hypothalamic and pituitary obesity are identical, and the author regards lipodystrophy as a variant of them.

Barcroft, J. (1934) *Features in the Architecture of Physiological Function*, Cambridge

Lichtwitz, I. (1939) *Bull. N. Z. Acad. Med.*, 2nd ser., **15**, 733

Meyer, H. H. (1931) *Deutsch. med. Wschr.*, **157**, 1531

Acute Hypophysial Necrosis

During the Puerperium

C. F. Brown and I. F. Idei report a case of acute hypophysial necrosis in the puerperium. The patient had hypertension and albuminuria during the later weeks of the pregnancy. Because of poor uterine contractions the patient was delivered with forceps after about 16 hours of labour. The placenta was retained and 1½ hours later the patient collapsed but was revived with a blood transfusion and intravenous fluids, and the placenta was then expressed. The patient's general condition was poor after delivery, blood-pressure remained low, she complained of headache, vomited a good deal, became drowsy, cyanotic, and died 93 hours after delivery. Necropsy showed necrosis of the anterior pituitary due to thrombosis. No bacteria were found nor were adrenotrophic or gonadotrophic hormones. The thrombosis causing the necrosis is ascribed to changes in the fibrinogen content of the blood during pregnancy. The retention of the placenta in this case would aggravate that change for a longer period. It is suggested that it is impossible to maintain life if the pituitary hormones are suddenly cut off, and that this condition is a commoner puerperal complication than is usually recognized.

H. C. Gotshalk and I. L. Tilden also report a case of necrosis of the anterior pituitary following parturition. If the patient survives this condition she often develops symptoms of Simmonds's syndrome. The patient, a woman, aged 26 years, who had had a previous pregnancy terminated spontaneously during the sixth month, was delivered spontaneously of a normal child after a labour of 27½ hours. The placenta and membranes were expressed 6 minutes later, but the uterus did not contract at first and the patient lost between 600 and 800 c.c. of blood. The loss continued, but more slowly, and her blood-pressure became very low. She had a cervical tear. In spite of 4 blood transfusions her blood-pressure remained as low as 80 mm. Hg systolic and 55 mm. Hg diastolic. She became cyanosed, twitching

developed, her temperature rose, and she died 67 hours after delivery. At the necropsy normal post-partum condition of the reproductive organs was found, except for the presence of 2 small cervical tears. Microscopical examination revealed necrosis of the anterior pituitary, marked hyperplasia was also present. During pregnancy the pituitary becomes hypertrophied and rich in blood. The sudden fall in blood-pressure after the delivery probably removed so much blood from the pituitary that necrosis began at once. The authors lay stress on the importance of maintaining the post-partum blood-pressure at its normal level in order to prevent such tragic results.

Brown, C. L., and Eder, I. I. (1939) *Amer. J. med. Sci.*, **198**, 166.

Gotschalk, H. C., and Tilden, I. L. (1940) *J. Amer. med. Ass.*, **114**, 33.

Tumours

Adenomas

Extrasellar extension.—G. Jefferson devotes his presidential address at the Neurological Section of the Royal Society of Medicine to the suprasellar extensions of pituitary adenomas, a condition widely recognized but never defined, and to the correlation of the extensions with different clinical pictures. The term extension should be applied to the condition of any exceptionally florid adenoma, when once its restraining bonds are broken, where it extends widely in all directions, is hour-glass or irregular in shape, and where the extrasellar portion is at least as large as, and almost always larger than, the intrasellar portion. The pituitary adenomas retaining a globular form with equal diameters should be called 'massive'. Among his 128 pituitary adenomas 18, or 14 per cent, showed extensions, and in Cushing's 365 adenomas the percentage was the same (Henderson). Every enlargement of the pituitary encroaches on the neighbouring tissues and may take place in all directions—downwards into the sphenoidal sinus, outwards to or into the cavernous sinus, upwards into the cranial chamber and then by further proliferation either in front of the chiasma into the anterior fossa, behind it into the third ventricle and hypothalamus, or below it laterally into the middle fossa. In the most exaggerated form the extensions occur in several directions at once and may reach the posterior fossa of the skull. The factors concerned in the production of extrasellar extensions are (i) the innate urge of the adenoma to enlarge progressively or intermittently, this is the most important, but the growth tendency of the cells of the adenomas varies greatly, and after activity may die out, (ii) the state of fixity of the chiasma, and (iii) the shape of the pituitary fossa and the nature of its diaphragm. The intracranial extensions are classified as hypothalamic (frontal, temporal, pharyngeal and posterior fossa), and are illustrated by accounts of cases. Malignant adenomas of the anterior pituitary retain the cellular structure of small tumours, but their malignancy is shown by cellular penetration of the capsule of the pituitary reaching positions where these cells would not be found normally. The term 'malignant adenoma' is regarded as somewhat artificial, but no other seems to be available, it is pointed out that 'malignancy' must be given a different valency in the various parts of the body, and that, although it might seem that in the case of pituitary adenoma 'massive extension' was only an alias for 'malignancy', this is not necessarily true. The influence of extension on the operative mortality in 98 cases with small pituitary adenomas the author's mortality rate was 2 per cent, whereas among 12 with extensions it was 4, or 33 per cent, as operation for cases with large extensions seemed to be a course of doubtful wisdom, other such cases were not operated upon.

Chromophobe adenomas.—L. M. Davidoff has summarized the main features of these, the commonest, tumours of the anterior pituitary. Two-thirds of the pituitary adenomas are composed of chromophobe cells, they appear in the third, fourth and fifth decades of life. The tumours are usually soft, brownish red, and reach a considerable size. The cells are elongated and columnar. The other endocrine and other glands are usually small, in contrast to the splanchnomegaly. Constitutional symptoms are as constant as pressure signs, and consist of amenorrhoea and in males loss of sexual libido and eventually of potency, atrophic changes in the skin, thinness and dryness of the hair, loss of axillary and pubic hair, the latter with a feminine distribution in males. In about 80 per cent of the patients there is an

abnormal obesity, the basal metabolic rate being low. The course of the disease is more rapid than in acromegaly, being seldom more than 10 or 15 years.

X-ray therapy - M. C. Sosman discusses the radiological treatment of pituitary adenomas, which may be used after their surgical removal or as the only form of therapy. Radiological treatment was given to 14 patients with a chromiophobe adenoma, 3 of the cases are described in detail, 2 were subsequently operated on, in 4 the condition was hopeless from the start owing to intracranial extension, and in 2 the treatment had been too recent to judge results. Of the remaining 8 patients, 7 were markedly benefited, vision improved and the general health and well-being was more normal. These improvements have been maintained for from 3 to 5 years with no relapses. The treatment fails when the growth is extensive, when pressure on the optic nerves has lasted long enough to cause atrophy, and when the tumour is cystic. The dangers of irradiation are the formation of adhesions between the chiasma and the tumour which prevent removal later if necessary, oedema of the brain (a very unlikely occurrence), and the slow response to the treatment which may allow the growth to go to dangerous limits before it is abandoned. L eosinophil adenomas causing acromegaly respond better than the chromiophobe adenomas to irradiation. The progress of the disease can be stopped by reasonable dosage, and it is a very efficient treatment for the headache which is so distressing to these patients.

Davidoff, I. M. (1940) *Bull. N. Y. Acad. Med.*, **16**, 239.

Henderson, W. R. (1939) *Brit. J. Surg.*, **26**, 811.

Jefferson, G. (1940) *Proc. R. Soc. Med.*, **33**, 433.

Sosman, M. C. (1939) *J. Amer. med. Ass.*, **113**, 1282.

Hyperpituitary Gigantism

Morgagni's Syndrome

R. I. Hemphill and L. Stengel give a full description of 3 cases, paranoid females, 31, 32, and 65 years of age respectively, with the condition described as 'Morgagni's syndrome' in 1927 by Henschen. A review of the 3 cases (1 necropsy) and of other reported examples showed that the syndrome consisted of diffuse hyperostosis of the vault of the skull without evidence of activity in the bone, diffuse degeneration, not senile, of the cerebral cortex mainly of the frontal and parietal lobes, widespread non-specific fibrosis of the lungs, and changes of a multi-glandular character in the pituitary, parathyroid, and thyroid; in the anterior pituitary there was an increased number of eosinophil cells with small eosinophil adenomas, the parathyroids showed signs of activity, and the thyroid some degree of atrophy, the last having a bearing on the obesity at one period in this patient and stated to be an important sign of the disease by some authors. It might be thought that the syndrome is a form of hyperpituitarism with a local giant growth.

Hemphill, R. I., and Stengel, L. (1940) *J. ment. Sci.*, **86**, 341.

Henschen, F. (1927) *Morgagni's syndrome*, Jena.

PITYRIASIS ROSEA

See also B. F. M. P., Vol. IX, p. 629.

Treatment

Convalescent Serum

H. D. Niles and M. M. Klumpp considered that, in view of the rarity of recurrence of pityriasis rosea, the serum of patients who had had the disease might possess immune properties. They therefore employed convalescent serum in 38 cases of the disease. When the supply permitted, 5 c.cm. were injected intramuscularly once, and occasionally twice, a week. Only one patient was given more than 3 injections. The patients soon became more comfortable and many stated that itching ceased after one injection. The duration of the eruption from onset to cure and from first treatment to cure was slightly shorter in patients treated with serum (3.9 weeks and 2.5 weeks), and slightly longer in another group of 50 patients

treated with ultra-violet light (5.3 weeks and 3.1 weeks), than in a group of 26 who received only mild antipruritic local applications (4.7 weeks and 3.1 weeks).

Niles, H. D., and Klumpp, M. M. (1940) *Arch. Derm. Syph., N.Y.*, **41**, 265.

PLAGUE

See also B.I.M.P., Vol. IX, p. 675, Cumulative Supplement, Key No. 1276; and Surveys and Abstracts 1939, pp. 148 and 479.

Prophylaxis and Treatment

Sulphathiazole

S. S. Sokhey and B. B. Dikshit report the effect of sulphathiazole on mice infected with plague. It was found that doses of 10 mg. twice daily for 10 days cures 80 per cent when given at the time of infection or during the following 24 hours before septicaemia has begun. If a dose of 40 mg. in a similar manner is given to mice 48 to 72 hours after their infection 80 to 90 per cent survive. Under experimental conditions sulphathiazole is a much more effective drug in plague infection than sulphapyridine.

Sokhey, S. S., and Dikshit, B. B. (1940) *Lancet*, **1**, 1040.

PLEURISY

See also B.I.M.P., Vol. IX, p. 699, and Cumulative Supplement, Key No. 1277.

Morbid Anatomy

Simultaneous Bilateral Pleural Effusions

B. I. Gordon reviews the incidence and mechanism of simultaneous bilateral pleural effusions. Simultaneous bilateral pleural effusions are rare, but occur in cardio-renal disease, and may occur as direct complications of bilateral artificial pneumothorax in the treatment of pulmonary tuberculosis. In a series of 259 cases of pleural effusion there was not any simultaneous bilateral effusion. Four cases of pulmonary tuberculosis and one case of a pleural new growth manifested simultaneous bilateral pleural effusion after intrapleural suction had been substituted for unilateral artificial pneumothorax on the originally treated side. It was concluded that the occurrence of fluid in the opposite or untreated pleural cavity in artificial pneumothorax cases is closely related to intrapleural suction employed to re-expand the collapsed lung, and that mechanical displacement of the mediastinum and stretching of the opposite lung cause a separation of the pleura, rupture of pleural lesions, and effusion. Great caution is necessary in dealing with a lung which has been collapsed for a long time, and expansion should be slowly induced under the control of reduced artificial pneumothorax, if this fails, thoracoplasty should be performed to bring the pleural surfaces into contact.

Gordon, B. I. (1939) *Trans. Ass. Amer. Phys.*, **54**, 157.

PNEUMONIA, LOBAR

See also B.I.M.P., Vol. IX, p. 713, Cumulative Supplement, Key No. 1279; and Surveys and Abstracts 1939, p. 479.

Prognosis

Significance of Eosinophilia

Because the differential leucocyte count to ascertain the prognosis of pneumonia takes much time and trouble, M. M. Bracken suggests that the eosinophil count alone might be used. From analysis of eosinophil counts on 180 cases, 60 of which were fatal, he found that eosinophils are not present in the blood early in severe cases, but may be in milder cases. Haemic eosinophilia is an index of recovery, although it may appear several days before any clinical improvement. Although

cosinophils may have been present, severe complications sometimes developed later. In patients dying of uncomplicated pneumonia eosinophilia is absent.

Bracken, M. M. (1939) *Amer. J. med. Sci.*, **198**, 386.

Treatment

Sulphonamide Drugs

Sulphapyridine — M. R. Reynolds and L. B. Slobody report on the method of use of sulphapyridine in the pneumonias of childhood. Dosage and the optimal time for discontinuing the use of the drug were the two clinical phases studied. The report is based on 75 cases ranging in age from 2 weeks to 11 years, about one-third were 2 years or younger. About 75 per cent were regarded as seriously ill on admission. A blood culture, complete blood count, and X-ray examination were made before beginning administration of the drug. Sputum or pharyngeal swabs yielded specific types of pneumococci in 32 cases. Type I, 10; Type IV, 4; Type VI, 5; Type VIII, 1; Type XI, 1; Type XIII, 1; Type XIV, 7; Type XVI, 1; Type XX, 1; Type XXIII, 1. Blood counts and urine analyses were made regularly during the entire stay in hospital.

In proportion to their body-weight, children tolerate relatively large doses of the drug, especially those under 2 years of age. The authors advocate the following scheme of dosage: For children under 2 years of age, 0.3 g. per kg. body weight during the first 24 hours, 0.15 g. per kg. during the second 24 hours, and on subsequent days. For children over 2 years of age, in cases of moderate severity 0.2 g. per kg. is recommended during the first 24 hours and 0.1 g. per kg. during subsequent 24-hour periods, and in severe cases 0.3 g. per kg. for the first 24 hours and 0.15 g. per kg. during subsequent 24-hour periods. From one-third to one-half of the first day's total drug should be given within the first 4 hours, the remainder is equally divided and given at 4-hour intervals both day and night. During the second 24 hours and thereafter one-half of the first day's total is given daily on a 4-hour schedule. Any case with bacteraemia should receive 0.3 g. per kg. in the first 24 hours and during the second 24 hours and thereafter 0.2 g. per kg. There was a striking drop in temperature and a rapid return to a state of well-being in all but 2 cases, the fall to normal temperature occurred in 8 to 30 hours, the average being 20, respirations usually remain accelerated and the child may appear toxic for 12 to 36 hours after the temperature falls. Signs of consolidation persist for about as long as would be expected in an untreated case. No deaths occurred and no empyema, although friction râles were heard in 4 cases of Type I infection, otitis media developed in 3 cases. The average stay in hospital was 11 days.

Two patients, aged 8 and 9, failed to respond to the drug, both showed on admission a markedly injected throat in addition to the pneumonic process, no pneumococci were obtained from either sputum. The authors state their opinion that the infecting organism in these 2 cases was not the pneumococcus. If satisfactory results are to be obtained from the use of sulphapyridine they will appear within 48 hours, provided the dosage is adequate.

As to the problem when the drug can be safely discontinued without the return of fever or toxicity, the authors adopted 2 tests, namely, the appearance of râles, and the return of normal respiratory rate. In several cases it was found that when the drug was stopped as soon as the temperature reached normal but while the respiratory rate was still accelerated, there was a return of temperature the following day. The most troublesome toxic manifestation was nausea and vomiting in 50 per cent of the cases, but this was never severe enough to stop administration of the drug, headache, dizziness, irritability, morbilliform rashes and cyanosis also occurred; leucopenia occurred in 2 children whose medication had been continued (in the early part of the study) until the fourth day of normal temperature.

D. S. Pepper *et al.* treated 400 cases of pneumococcal pneumonia with sulphapyridine. Of these cases, 104 were due to Type I pneumococcus and the mortality was 5.8 per cent, 30 were due to Type II with a mortality of 6.7 per cent, and 67 were due to Type III with a mortality of 16.4 per cent. One hundred cases of non-typed pneumonia were also treated. Most of the patients received 2 g. of the drug by mouth, followed by 1 g. every 4 hours until a total of 25 g. had been given. If the treatment was begun more than 5 days after the onset of the disease, a total of

15 g. was sufficient. A few patients with a positive blood culture received 50 g. in all. The average level of sulphapyridine in the blood during treatment was 4 to 6 mg. per 100 c. cm. In 381 of the cases the urine was analysed during the treatment to ascertain the extent of renal damage caused by the drug. During the acute stages of the disease 7 per cent had haematuria, but only 5.4 per cent had it after treatment had begun. In some cases the haematuria disappeared although sulphapyridine was still being given. In 12 fatal cases sections of the kidneys were examined but there was no constant change which could be ascribed to the drug. The most striking effect of the treatment was the rapid drop in temperature, usually by crisis. This was followed by an improvement in the toxæmia and general health of the patient. In most patients there was also a rapid fall to normal of the total white blood-cell count. In this series there were 5 cases of empyema and 11 cases of large pleural effusion. Toxic reactions to the drug occurred, nausea and vomiting being the most frequent. In 25 patients the vomiting was so severe that the drug had to be stopped. Many measures were employed to prevent this reaction and the giving of sodium chloride and dextrose intravenously was the most successful. Other toxic reactions such as cyanosis and drug fever occurred and one patient developed acute haemolytic anaemia.

In the 100 non-typed patients the effect of the drug was difficult to evaluate, in some it had little or no effect. The authors concluded that sulphapyridine is a useful drug in the treatment of pneumococcal pneumonia and there was not one death in all the 500 cases which could be attributed to its use.

C. H. Smith and R. I. Nemir treated 79 children with lobar pneumonia, 11 with broncho-pneumonia, 1 with lobular pneumonia, and 2 with 'subacute pneumonia' with sulphapyridine. On the first day 0.2 g. per kg. of body weight was given, on the second day half this amount was given. Most children of over 2 years of age were found to do well on three-quarters of this dosage, but infants needed the full dosage. Most of the cases required treatment for only 2 or 3 days. In those examined the blood concentration was found to vary widely in different children receiving the same dose. A very low blood-concentration was noted in some patients, although they had a crisis 18 hours after the drug was given. Vomiting was the most frequent toxic reaction. Delirium resulted in 4 children whose blood concentrations were very high. Of 79 patients with lobar pneumonia 69 had a crisis within 18 to 24 hours. In 5 other cases the crises did not occur for 48 hours. In the cases of broncho-pneumonia the response was not good and 4 of the children died. The authors stressed the importance of stopping the drug after it had produced a crisis, because prolonging the treatment may add to toxic cumulative effects.

J. P. Scott treated 58 infants and children suffering from pneumonia with sulphapyridine, 56 similar cases were studied as controls. In many cases in both groups pneumococci were found in the sputum. All the patients received the same treatment, except that sulphapyridine was omitted in the control group. None of the patients received specific serum. The dosage given was 1.5 grains of sulphapyridine per pound of body weight, divided into 6 or 8 doses daily. Treatment was continued for 96 hours, unless toxic reactions occurred. The commonest toxic reaction was vomiting. In the treated group the temperature dropped on an average nearly 3 days sooner than in the untreated group. There were 2 deaths in the control group and none in the treated group, when the dosage was adequate. Five moribund infants were given sulphapyridine. Three died, but 2, who received adequate amounts, recovered.

O. Romeke and E. Vogt reported the results of treating 342 cases of pneumonia with sulphapyridine, 245 of the cases were lobar and 88 atypical pneumonia, the latter being mostly broncho-pneumonias. The mortality-rate in this series was 8.3 per cent. If those dying within 24 hours of admission to hospital were excluded it was 5.8 per cent. For the lobar pneumonias the mortality-rate was 4.3 per cent. The mortality-rate was lower the earlier the patient was admitted to hospital. The majority of the infections belonged to Types I, III, and VII. The average total dose of the drug given to those over 10 years of age was 22 g. The response to the drug was usually rapid and in only 5 cases in the whole series was there no response. Pleural effusion, otitis, and empyema were the commonest complications. Toxic effects from the drug were noted, but very few were serious. Cyanosis, vomiting, drug fever, leucopenia, and in one case agranulocytosis occurred.

N. Plummer and H. K. Insworth treated 270 patients suffering from pneumococcal pneumonia, either typical (lobar) or atypical pneumonia, with sulphapyridine. The routine initial dose was 2 g. followed by 1 g. every 4 hours until 16 g. had been given. After this the drug was stopped, reduced or increased according to the progress of the disease. Most of the patients needed an increased dosage. The pulse-rate and temperature dropped rapidly in most cases, and the mortality-rate was greatly reduced, only 34 patients dying in this series. There were no serious toxic reactions, but nausea and vomiting were common. Complications occurred but rarely, they included empyema, otitis media, and pleural effusion. Examination of the blood showed that it was quickly sterilized by the drug. The drug was well absorbed, but there was no constant blood-level, nor could the blood-level be correlated with the changes in the clinical condition.

T. J. Abernethy *et al.* employed sulphapyridine by mouth in 110 cases of pneumococcal pneumonia, and sodium sulphapyridine intravenously with sulphapyridine orally in 25 cases of pneumococcal pneumonia. In the first few cases sulphapyridine was given in a dosage of 2 g. followed by 1 g. four-hourly thereafter until the temperature had been normal for 48 to 72 hours. The dosage was then reduced to 1 g. every 6 hours for 48 to 72 hours, then to 0.5 g. every 4 hours for a similar period. Sodium sulphapyridine was given intravenously as a 5 per cent solution in distilled water or physiological saline. The usual dosage was 3.8 g. for undersized patients 0.05 g. per kg. of body weight was given. In the entire group of patients the mortality rate was 11.1 per cent; in 99 non-bacteraemic cases the rate was 8 per cent, and in 23 bacteraemic cases it was 21 per cent. No deaths occurred in 23 Type I infections.

W. I. Whittemore *et al.* treated 92 cases of pneumococcal pneumonia with sulphapyridine. To 14 of the patients the drug was given per rectum and to 18 intravenously. The intravenous dose was usually 2 g. in 20 c.cm. of normal saline. Rectally 6 g. suspended in 3 ounces of water containing 0.66 to 1 g. of sodium bicarbonate were given. It was given as a retention enema after a cleansing enema. In both groups the results were good, although the blood-level of the sulphapyridine was lower in the group which received it rectally. There was no nausea in this group. In the intravenous group nausea occurred after injection in one case. The response to the drug in this group was very rapid but somewhat erratic. In the 92 cases 7 deaths occurred, and these cases were reported in detail. The authors considered that the most desirable method of giving the drugs to those who are seriously ill is first intravenously then orally. If there is no response to the drug specific serum should be given in every case.

Sodium sulphapyridine intravenously. M. Finland *et al.* (1940, b) reported on the intravenous administration of sodium sulphapyridine in 21 patients with severe infections, as a preliminary to the oral use of sulphapyridine. In each case sterile physiological saline was employed as diluent. The amounts of the drug in each injection varied from 2.5 to 5.0 g., given in from 80 to 2,000 c.cm. of saline, or in concentrations of from 0.2 to 5 per cent. For the most part a 1 per cent solution was used, the larger volumes being reserved for dehydrated patients. When a volume of 100 c.cm. or less was given, it was injected from a syringe in from 10 to 20 minutes, larger volumes were given by a slow drip, in from 1 to 24 hours. One of the patients received 7 injections, 3 were given 2, and the others one. The maximal concentrations, reached a few minutes after the end of the initial injection of 4 or 5 g. of the drug, ranged from 8.6 to 12.4 mg. per 100 c.cm. The most usual toxic effect was nausea, with or without vomiting, and generally began during the injection, and lasted several hours. In 9 of the patients there were no untoward reactions of any kind. In view of the severity of the cases, which included pneumococcal meningitis, and pneumococcal pneumonia, the therapeutic effect of the drug was difficult to assess, but the authors concluded that intravenous sulphapyridine is of therapeutic value, and may be life-saving in selected cases. A highly-concentrated solution of sulphapyridine in 50 per cent glucose was also employed in a group of cases. It was found to be non-toxic when given parenterally, but, given thus, was generally merited.

Soluble sulphapyridine. -W. I. Garford *et al.* stated that the chief drawback to the use of sulphapyridine in the treatment of pneumonia is its liability to cause vomiting. They reported 29 cases of pneumonia or broncho-pneumonia due to

the pneumococcus, 2 cases of influenza, one of rheumatic fever, and one of pneumococcal meningitis in which the drug was given intramuscularly to 27 patients and intravenously to the remaining 6. The usual intramuscular dose was 3 c.cm. of the 33 per cent solution of sulphapyridine soluble every 3 or 4 hours. Intravenously, this dose was made up to 10 c.cm. with distilled water or saline. In children the doses varied from 0.15 to 1.0 g. according to age and no ill-effects were noted. Twenty-five of these cases recovered and in only 4 of them did vomiting occur. The case of pneumococcal meningitis proved fatal. The authors suggested that in giving sulphapyridine, four to six injections of 3 c.cm. should be given at 4-hourly intervals, then followed by small oral doses which are less likely to induce vomiting even in susceptible persons.

Sulphapyridine and barbiturates. J. Adriani found that rats treated with sulphanilamide were highly susceptible to the action of the barbiturates. He concluded that it might be unwise to give the two drugs together in the treatment of humans. These observations led W. L. M. King to review 30 cases of pneumonia which had received sulphapyridine or sulphanilamide. Of these cases 18 had also received a barbiturate as a sedative. Nembutal was the commonest sedative used, then sodium amytal. Only one untoward reaction occurred. A pregnant woman had 6 grains of sodium amytal, after which she could not be roused for 18 hours. These 30 cases showed the good clinical improvement which follows sulphapyridine treatment. There were 4 deaths in this series, 3 of them showing that sulphapyridine is not so effective in the treatment of pneumonia caused by a mixed streptococcal and pneumococcal infection as in the treatment of pneumonia caused by pneumococci alone.

Sulphapyridine and hydroxyethylapocupreime dihydrochloride. M. L. Menten *et al.* investigated the relative merits of sulphapyridine and hydroxyethylapocupreime dihydrochloride in pneumonia. Seventy-nine patients were divided into 3 groups, one of these drugs being administered to each of the first two groups, and the third group receiving only symptomatic treatment. The usual dosage of sulphapyridine was 0.15 g. every 4 hours for infants 1 to 3 months old, and 0.9 g. for children of 12. The dosage of hydroxyethylapocupreime varied widely, the total amount given ranging from 3 g. to 38.3 g. While it was difficult to reach definite conclusions, the authors gained the impression that the course of the disease was appreciably shortened with these drugs when pneumococci only were present. Their value was open to question in mixed infections.

Sulphapyridine and serum. C. S. D. Don *et al.* studied the effect of sulphapyridine with and without serum in the treatment of 234 cases of lobar pneumonia. The series was adequately controlled and blood cultures, pneumococcal typing, and leucocyte counts were carried out. The dosage of the drug used was 2 g. by mouth, followed by 1 g. 4-hourly until 24 hours after the temperature had fallen to normal. This treatment was restarted if the temperature rose again. Typing was done within 24 hours of admission, and patients under 40 years of age received 50,000 units of serum intravenously. All other patients received 100,000 units of serum. No additional doses of serum were given. No sensitivity tests were done and adrenaline was given if rigors or dyspnoea developed. In 78 control cases there were 21 deaths. In 119 cases treated with sulphapyridine alone there were 8 deaths. In 37 cases of either Type I or Type II pneumonia treated with specific serum and sulphapyridine there were 3 deaths. The authors considered the figures too small to draw conclusions about the value of specific serum. Sulphapyridine halved the mortality of cases with positive blood cultures. Complications were rarer after the use of the drug than in the controls, though they confirmed Anderson and his co-workers' observation that the forced crises effected by sulphapyridine did not always produce the same brightness that follows the true crises. The drug had no effect on the speed of resolution of the consolidated lung.

M. Finland *et al.* (1940, a) made clinical and laboratory studies in 1,037 cases of pneumococcal pneumonia to evaluate the relative merits of serum and sulphapyridine. They concluded that both sera and sulphapyridine are highly effective agents in the treatment of pneumococcal pneumonias. Laboratory studies suggested that the combination of serum and sulphapyridine was the optimal form of treatment. Either of these 2 agents, when used alone, was about equally effective. Cases in which the combined treatment was most effective included bacteraemic patients,

especially those over 50, patients in whom treatment was begun late in the disease, and patients whose blood cultures yielded moderate or large numbers of pneumococci, most patients over 60 years of age who had more than a mild infection, and patients with Types II, III and possibly V infection, except in mild cases. In treating pneumococcal pneumonia, it is advisable to begin with sulphapyridine as soon as the clinical diagnosis has been made, but only after blood has been taken for culture and every effort has been made to obtain sputum for typing. In severe cases, falling into the above categories, specific serum should be given as soon as the causative types have been determined, or the results of blood cultures have become known. In patients also in whom continued drug therapy may prove harmful as in renal and hepatic disease, severe anaemias and blood dyscrasias serum should be used as soon as the type is known. In all other cases due to specific types of pneumococci, serum should be used if there is no satisfactory response to the drug after 24 to 36 hours. In cases treated early in the disease, serum may be preferred, particularly if the drug is not well tolerated.

Evaluation of sulphathiazole and sulphapyridine. H. F. Flippin *et al.* investigated the relative therapeutic values of sulphathiazole and sulphapyridine in pneumococcal pneumonia. In a series of 100 cases of typed pneumonia, sulphathiazole was given in the following dosage, an initial dose of 3 g. by mouth was repeated in 4 hours, then followed by 1 g. every 4 hours. This maintained a blood concentration of the drug of 5 mg. per 100 c.c.m. Treatment was continued until the temperature remained normal for 48 hours, and there was evidence of clinical improvement. In general the total dosage was 25 to 40 g. Equal amounts of sodium or potassium citrate were given with each dose of the drug. In another comparable series of 100 cases of pneumonia sulphapyridine was given in the following dosage: the initial dose was 3 g. by mouth, followed by 1 g. every 4 hours until a total of 25 to 35 g., according to response, had been given. Equal amounts of sodium bicarbonate were given with each dose of the drug. Of the patients treated with sulphathiazole, 12 died. Excluding cases which were moribund on admission the mortality for the sulphathiazole group was 7.5 per cent, and for the sulphapyridine group 11.4 per cent. The authors concluded that sulphapyridine brings down the temperature somewhat more rapidly than sulphathiazole, although the average number of days of hospitalization in the 2 groups was the same, 13.2 days. Nausea and vomiting were much less frequent and severe in patients treated with sulphathiazole than in those treated with sulphapyridine. Other toxic manifestations were approximately equal in the 2 groups, and were not severe.

Oxygen

A. M. Burgess agrees that oxygen therapy is an accessory method of considerable value, and is sometimes indispensable, in lobar pneumonia. Its chief value is for the relief of the harmful effects of anoxia, particularly on the nervous and cardiovascular systems. The most important clinical sign for determining the presence and degree of anoxia in pneumonia is the presence of cyanosis, but severe dyspnoea, even in the absence of cyanosis, also indicates the use of oxygen. At the Rhode Island Hospital, during a period of 3 years, approximately 50 per cent of all patients with lobar pneumonia received oxygen, either through a nasal catheter or by open box. In patients with much abdominal distension unrelieved by ordinary methods, 95 to 98 per cent oxygen, given by the closed-box method, often gave relief.

Procaine Injection for Relief of Pleuritic Pain

S. Schnur endeavoured to relieve the pleuritic pain of early pneumonia by the injection of 5 to 10 c.c.m. of 2 per cent procaine hydrochloride (novocain) intracutaneously, subcutaneously, and intrapleurally into the intercostal spaces surrounding the position of maximal intensity of the pain. Piercing the parietal pleura with a hypodermic needle seemed to give the best results. In the 31 cases of pneumonia in which the treatment was tried, 25 experienced complete relief, and in 6 some soreness remained. Of the 25, 18 showed no recurrence, while in the remaining 7 the pain returned at periods ranging from 5 minutes to 26 hours. Five of the latter cases were eased by strapping or narcotics, and the other 2 reinjected, the relief thus secured still being incomplete. These injections eased the cough, aided respiration, and secured rest. They had no effect in preventing the

subsequent development of such complications as an extension of the consolidation to other lobes, pleural effusion, or pneumothorax.

X-Rays

L. Solis-Cohen and S. Levine employed X-irradiation in 20 adults and 22 children with pneumonia. Of the adults 9 received a dosage of 150 to 200 r, and 11 received 300 to 400 r. Of the children 15 received 200 to 300 r, and 7 received 150 r. In adults thus treated 4 died (20 per cent) as compared with 25 per cent in a series of 40 who received no irradiation, and 7 of whom were treated with serum. Of the children, 1 died, as compared with 1 death in a series of 21 children who received no irradiation. The irradiated children, however, were comfortable and did not develop complications, and passed through a less stormy course than the children who were not irradiated. Complications such as empyema, pleural effusion, and otitis media in convalescent patients were not averted by X-irradiation, nor was bacteraemia prevented.

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 Plummer, N., and Lasworth, H. K. (1939) *J. Amer. med. Ass.*, **113**, 1847.
 Reynolds, M. R., and Slobody, I. B. (1939) *Arch. Pediat.*, **56**, 415.
 Romcke, O., and Vogt, E. (1939) *Lancet*, **2**, 778.
 Schuur, S. (1939) *Ann intern Med*, **13**, 845.
 Scott, J. P. (1940) *Amer. J. Dis. Child*, **59**, 711.
 Smith, C. H., and Nemer, R. E. (1939) *J. Amer. med. Ass.*, **113**, 1857.
 Solis-Cohen, L., and Levine, S. (1939) *Amer. J. Roentgenol.*, **42**, 411.
 Whittemore, W. L., Royster, C. L., and Riedel, P. A. (1940) *J. Amer. med. Ass.*, **114**, 940.

PNEUMOTHORAX, SPONTANEOUS

See also B.E.M.P. Vol. IX, p. 743. Cumulative Supplement, Key No. 1280, Surveys and Abstracts 1939, p. 484.

Clinical Picture

Systolic "Clicks"

J. G. Scadding and P. Wood report 4 cases of shallow left-sided spontaneous pneumothorax in which clicking extra sounds were heard in the cardiac cycle. Two other cases of left-sided artificial pneumothorax in which they were heard are also reported. The sound was systolic and best heard at the apex. Sometimes a less distinct diastolic click was audible and occasionally complex extra clicks during systole. The sound was not heard in patients with a larger pneumothorax. Small changes in posture altered the intensity of the sound, which must be differentiated

from the crackling sounds heard in mediastinal emphysema. They are probably made by the forcible separation of the visceral and parietal pleurae during the cardiac systole. The condition can be differentiated from systolic gallop rhythm, because in this condition the additional sound resembles the first heart sound.

Scadding, J. G., and Wood, P. (1939) *Lancet*, **2**, 1208

Valvular Pneumothorax

F. G. Chandler stated that the majority of cases of spontaneous pneumothorax are non-tuberculous in origin, but he stressed the importance of an exhaustive history and clinical examination in every case to eliminate the possibility of tuberculosis. He reported a case of recurrent spontaneous pneumothorax successfully treated with induced obliterative pleurisy. The patient had had 10 attacks induced by the most trivial acts. Both the right and left side had been affected. The eleventh spontaneous pneumothorax occurred on the right side, and Chandler induced pleurisy by injecting 5 c.cm. of a 10 per cent solution of gomenol in olive oil through a thoracoscope, at the same time withdrawing 1,800 c.cm. of air. The lung re-expanded successfully and, although it is impossible to say how firm the adhesions between the two layers of the pleura are, it is proposed to repeat the treatment on the left side should a spontaneous pneumothorax occur there. Chandler also reported a case of high pressure pneumothorax with a valvular tear, which he successfully treated with induced pleurisy combined with the Zachary-Cope self-retaining cannula fitted with a mechanical valve which allowed the air to come out of the pleural cavity again, and therefore the lung re-expanded and the mediastinum resumed its normal position.

Chandler, F. G. (1939) *Lancet*, **2**, 638

Treatment

Simple Apparatus for Constant Suction

H. L. Marriott and A. F. Foster-Carter describe a simple apparatus to maintain a constant low pressure in spontaneous pneumothorax. A large bottle, capable of holding at least 80 ounces of fluid, with a straight outlet tube at the bottom provided with a tap is used; the cork of the bottle is pierced by a tube reaching below the level of the water and can slide in the cork so that its height can be altered. When the tap at the bottom is opened, water flows out of the bottle, and air is drawn through the tube. If the tube is connected to a closed cavity, negative pressure develops within it. The pressure produced is proportional to the height of the lower end of the tube above the level of the outflow; that is, if the distance is 10 c.cm., a negative pressure of 10 c.cm. of water will develop in the closed cavity when the tap is opened. When the apparatus is in use for the treatment of a spontaneous pneumothorax, the tube is attached to a needle inserted into the chest, and a manometer to measure the pressure can be incorporated in the apparatus. The authors report 2 cases with an artificial pneumothorax induced for pulmonary tuberculosis, in which this apparatus was used to remove excess air which distressed the patient. This method has the advantage that the negative pressure can be made so small that almost no pull is exerted on the lung.

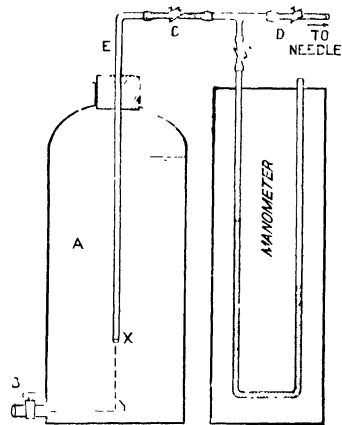


FIG. 12. Diagram of apparatus for maintaining constant suction in spontaneous pneumothorax. (From *Lancet*, 1940)

Marriott, H. L., and Foster-Carter, A. F. (1940) *Lancet*, **1**, 122

POLIOMYELITIS AND POLIOENCEPHALITIS

See also B I M P., Vol. X, p 12, Cumulative Supplement, Key No 1282, and Surveys and Abstracts 1939, pp. 42 and 484.

Aetiology*Infected Drink-Water*

On April 12, 1940, when postal and other means of communication with Scandinavia were difficult, C Levaditi received for report to the Académie de Médecine of Paris a wireless message from C. Kling of Stockholm to the effect that specimens of faecal-contaminated water had been shown to contain the virus of acute poliomyelitis. It appeared that in August, September and October, 1939, there was an epidemic of 70 cases of that disease in Stockholm, and that from water contaminated by faeces acute poliomyelitis had been produced in monkeys by intraperitoneal and intrasciatic inoculation.

Levaditi, C (1940) *Bull. Acad. Med. Paris*, **123**, 335

Bacteriology*Animal Susceptibility to Virus*

C Armstrong points out that, although until recently the only practical experimental animal has been the monkey which is not, for several reasons, an ideal laboratory animal, it has been shown (1939) that the Eastern cotton rats and mice are susceptible to the Lansing strain of poliomyelitis. The virus has now been carried through 27 consecutive transfers in the cotton rat, and later 13 successive mouse transfers were carried out, the animals uniformly showing a flaccid paralysis and morbid changes similar to those in human poliomyelitis.

Armstrong, C (1939) *Publ. Hlth Rep., Wash.*, **54**, 1719

(1940) *Trans. Coll. Phys., Philad.*, 4 ser., **8**, 8

Diagnosis and Differential Diagnosis*New Intradermal Test*

I C Rosenow described a new intradermal test for acute poliomyelitis. He investigated 271 cases of the disease, 150 contacts, and 767 controls who gave no reaction to normal horse-serum. Intradermal injections were given of 0.03 c.c. of a 10 per cent solution of the water-insoluble fraction of the serum of horses hyperimmunized with streptococci from poliomyelitis. The same material prepared with streptococci from diseases other than poliomyelitis and normal horse-serum were used as controls. A positive reaction was shown by erythema beginning almost immediately after the injection, reaching its maximum in 5 to 10 minutes, and then fading from the periphery. The reaction was greatest in degree and incidence in those having poliomyelitis, next among contacts, then among controls within epidemic zones, and least of all in controls outside epidemic zones. The reaction to the serum prepared from streptococci associated with other diseases had about the same incidence, but was much less. In those in whom the poliomyelitis euglobulin gave a positive reaction streptococci were found in the nasopharynx which produced flaccid paralysis in animals. This was not so when the skin test was negative. The fraction of the serum producing the positive skin reaction appears to be an antibody.

Rosenow considered the test to be diagnostic of clinical and sub-clinical anterior poliomyelitis, and that it showed that the streptococcus is as much an active part of the infection as the virus to which it is usually attributed.

Rosenow, I C (1939) *Proc. Mayo Clin.*, **14**, 734

Treatment*Prontosil Soluble*

W M Rhett employed neoprontosil (prontosil soluble) in 440 acutely ill children during an epidemic of poliomyelitis. The approximate average dosage employed was 1 gram per pound of body weight daily, given in divided doses every 3 to

4 hours. This dosage was generally given day and night until fever and toxæmia had subsided for a period of 24 hours. The midnight dose was then omitted, but the other doses were continued over a period of 7 days from the onset of the illness. When positive central nervous system symptoms were present, or when the disease was strongly suspected, the full dosage was continued for a longer period (until subsidence of symptoms), and then it was tapered off as in streptococcal infections. Of these children only one developed paralysis; this was a transient paralysis, developing on the fifth day, in a child whose mother had not kept up the maintenance dose of the drug. Symptoms subsided when full dosage was resumed. Two other children developed meningeal symptoms on the fifth day of the illness, and in these cases also the maintenance dose had been discontinued. On resumption of the full dosage of the drug symptoms subsided without paralysis. In 14 cases of poliomyelitis neoprontosil was given during the preparalytic stage, and only one, referred to above, developed paralysis. Eight cases in which a clinical diagnosis of meningeal involvement was made subsided with neoprontosil medication without paralysis. In 11 patients with paralytic involvement, toxic symptoms subsided in from 24 to 48 hours, and there was no apparent advance in paralytic involvement after adequate dosage of the drug had been reached and held for 24 to 48 hours. There were no deaths in the acute phase of the disease.

Potassium Chlorate

J. Saucier and O. W. Stewart carried out a series of experiments which repeated as exactly as possible the work of Contat *et al.* who claimed to have obtained evidence of a specific protective action of potassium chlorate against experimental poliomyelitis in monkeys. Three groups each consisting of 4 rhesus monkeys were employed, each group being inoculated with different strains of the virus of poliomyelitis obtained from the spinal cords of infected monkeys. One group of the monkeys was then given 0.1 g. of potassium chlorate per kilo of body weight by mouth, this being given in 12 divided doses 2-hourly. In the other 2 groups of monkeys this dosage was doubled. Of the first group, one animal developed typical poliomyelitic lesions of the cord at autopsy. Temperature elevation occurred in members of the second group. All 4 members of the third group developed the disease. In spite of the failure of members of the first 2 groups to develop the disease, which the authors attributed to either low potency of the virus employed or to resistance of the animals, the definite conclusion reached was that potassium chlorate was of no value in preventing the development or influencing the course of poliomyelitis.

Contat, C. (1938) *Schweiz. med. Wschr.*, **68**, 669

— Arthus, M., Spycher, C., and Debat, F. (1939) *Ann. Thér. biol.*, p. 7.

Saucier, J., and Stewart, O. W. (1940) *Canad. med. Ass. J.*, **42**, 19.

Rhett, W. M. (1940) *J. Pediat.*, **16**, 326

PREGNANCY: NORMAL AND PATHOLOGICAL

See also B.E.M.P., Vol. X, p. 48; Cumulative Supplement, Key Nos. 1291-1303; Surveys and Abstracts 1939, pp. 29 and 488; and p. 17 of this volume.

Physiology

Changes in Maternal Organs during Pregnancy

Endometrium—S. H. Sturgis describes the characteristic changes in the endometrium in early pregnancy. In 7 patients investigated 6 weeks after their last period, pregnancy was not suspected by either the patient or her doctor, but biopsy indicated its presence. Among 1,500 biopsies, taken for various gynaecological reasons, 11 showed an unusual pattern of secretion in the endometrial glands. Of these, 10 subsequently proved to be pregnant. The secretory activity described may be the only diagnostic sign present. Under a low-power lens the glands appear saw-toothed in longitudinal section and star-shaped in transverse. They were crowded together in the spongy layer of the endometrium. Under the high power the epithelial cells lining the glands were seen to be swollen and filled

with coarse, deeply-staining granules. The nuclei were round and lightly-staining, and there were no mitoses. The biopsy, when carefully made, did not necessarily interfere with early pregnancy. In this series, they were done with a sharp-tipped retraction curette. The specimen, of about 5 c mm. of tissue, was usually taken from the region of one or both cornua.

Hormones in Pregnancy

Thyroid gland G. Mascia discusses the changes which the thyroid shows in pregnancy, the puerperium, and lactation. During pregnancy the thyroid follicles increase in size, number, and colloidal content. Later in pregnancy and during lactation a considerable hyperaemia and hyperplasia is noteworthy. The findings of the author were not uniform and further experimental evidence is needed to establish exact correlation.

Mascia, G. (1939) *Ann. Ostet. Gynec.*, **31**, 945.

Sturgis, S. H. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 10.

Diagnosis

Modification of Aschheim-Zondek Test

R. I. Kelso describes a 24-hour modification of the Aschheim-Zondek test for pregnancy. In the original test immature female mice are employed, and the test takes 96 hours. In the Friedman test adult female rabbits are employed, and the test takes 48 hours; its disadvantages are the need for intravenous injections, the use of a single animal which may be refractory, and the cost of the rabbit. In Kelso's test 4 immature rats are employed, 2 being examined after 24 hours, and 2 after 72, these 2 being used as controls. Doses given vary from 0.5 to 2.0 c cm. of urine, according to the specific gravity. Both ovaries must be enlarged and hyperaemic to be regarded as positive. About 4 per cent of cases gave false positives in the 24-hour rats, but true negatives in the 72-hour rats. The 72-hour rat test is as accurate as the Aschheim-Zondek or Friedman tests.

Friedman Test

I. M. Randall *et al.* analysed 645 Friedman tests carried out at the Mayo Clinic. Of these, 302 gave positive results, 10 of which, as shown subsequently, occurred in the absence of pregnancy, and 343 gave negative results, 7 of which were obtained when pregnancy was actually present. Thus in 2.63 per cent of the tests the result was at variance with the ultimate diagnosis. In most cases a diagnosis of the presence or absence of pregnancy could not be determined definitely by history and physical examination when the Friedman test was performed. The authors pay special attention to the relatively small group of reactions which did not agree with the actual presence or absence of pregnancy. They point out that the test is based primarily on the fact that, if anterior pituitary-like hormones are present in the urine in certain amounts, they will produce typical changes in the ovary of the rabbit, and that it is a quantitative test. The presence in the urine of the gonadotrophic principle in excessive amounts may be responsible for a positive Friedman reaction in the absence of pregnancy. Among the several pathological and physiological states other than normal pregnancy which may give a false positive reaction are hydatidiform mole, chorionepithelioma, menstrual disorders, such as primary ovarian failure, the menopause, treatment with preparations of anterior pituitary, and errors in technique. A negative reaction with the Friedman test before the seventh week after the last menstrual period may not be conclusive, although authentic positive reactions may be obtained much earlier, often within 4 weeks after impregnation. A test which gives negative results before the seventh week should be repeated later.

The Pregnotin Test

H. H. Pevaroff and L. H. Biskind report on an examination of 48 women by the pregnotin test for pregnancy. The test is made with an antigen prepared from the human placenta, and is given by intradermal injection. The reaction was positive in 21 out of 22 women known to be pregnant. A control solution is first injected to form a bleb, 5 minutes afterwards, 0.1 c cm. of the test solution is injected in a parallel location. If pseudopodia appear at the margin of the bleb in from 1 to 4

minutes, the test is positive. Seven post-natal patients all gave a positive reaction up to 12 days after delivery. Two out of 6 males gave a positive result, possibly due to deterioration of the test solution. One of 10 definitely not pregnant patients gave a positive result. The test was used for diagnosis in 3 cases, the result being correct in 2 of them.

Pevaroff and Biskind conclude that the test is the best of all skin tests for pregnancy. It is useful for rapid diagnosis, but it should always be confirmed by the Aschheim-Zondek or Friedman tests, with which it could not be compared for reliability.

Cold-Pressor Test

L. C. Chesley and E. R. Chesley carried out cold-pressor tests during the third or early fourth month of pregnancy, during the eighth or early ninth month of pregnancy, and 6 weeks or more after pregnancy, in a series of 517 women. They found that the response was inconstant, and that it was independent of family history, of cardiovascular renal disease, and of diabetes. It was also independent of age, gravidity, weight, weight-height index, weight gain in pregnancy, and perhaps also of basal blood-pressure. The incidence of toxæmia was essentially the same in both normal and hyper-reacting groups.

Chesley, L. C., and Chesley, E. R. (1939) *Surg. Gynec. Obstet.*, **69**, 436.

Kelso, R. F. (1940) *Amer. J. Clin. Path.*, **10**, 293.

Pevaroff, H. H., and Biskind, I. H. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 315.

Randall, L. M., Magath, T. B. and Pansch, F. N. (1940) *J. Amer. med. Ass.*, **114**, 471.

Combined Pregnancy

According to A. Bernstein combined pregnancy, i.e. simultaneous extra-uterine and intra-uterine pregnancy, is not so rare as is supposed; up to the present 294 cases have been reported. This is a type of twin pregnancy, one fertilized ovum becoming implanted in the uterus and one in the tube, or rarely, in the ovary. The most common factor interfering with the passage of the fertilized ovum into the uterus is some inflammatory lesion of the adnexa. The mortality rate in the cases reported was 20.7 per cent. The maximal age incidence is 26 to 35, the active period of childbirth. The diagnosis is often difficult.

Bernstein, A. (1940) *Amer. J. Surg.*, **47**, 597.

Hyperemesis Gravidarum

Treatment

Adrenal cortex — W. N. Kemp in 1932 suggested that certain cases of nausea and vomiting in pregnancy might be due to adrenal cortical insufficiency because the cortex does not hypertrophy sufficiently rapidly to meet the new demand made upon it. He successfully treated a series of such patients with adrenal cortex. This led J. Kotz and M. S. Kaufman to treat 50 cases with adrenal cortex orally and subcutaneously. The therapeutic dose was based on the severity of the symptoms. For ordinary mild nausea of pregnancy, one 5 min. capsule (equivalent to $\frac{1}{2}$ rat unit as determined by the Grollman method), 3 times daily 15 minutes before meals, was given. In more severe types, there was given, with the capsules, 1 c.cm. (equivalent to $2\frac{1}{2}$ rat units) daily by subcutaneous injection. Most of the cases were benefited, and the author thought that the results were better than when anti-spasmodics, endocrines, or sedatives were used. In severe cases it was also necessary to employ measures to relieve the acidosis, etc.

Kemp, W. N. (1932) *Endocrinology*, **16**, 434.

— (1933) *Canad. med. Ass. J.*, **28**, 389.

Kotz, J., and Kaufman, M. S. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 449.

Toxaemias of Late Pregnancy

Aetiology

Hypovitaminosis-B₁ — A. C. Siddall advanced the hypothesis that a deficiency of

vitamin B₁ may cause altered function of the pituitary and give rise to the toxæmias of pregnancy. He gave to 20 cases of pre-eclampsia daily injections of 6.7 mg. of aneurine hydrochloride, for 10 days. Compared with control cases the injections were apparently without effect. However, it has been shown that eclampsia is commonest in districts where vitamin-B deficiencies, such as pellagra, are also seen. Likewise, it is commonest in February to April when the intake of fresh foods containing vitamin B₁ has been least during the winter months. Siddall stated that, to be of any use in the prevention of toxæmia, vitamin B₁ must be given throughout the whole of pregnancy and lactation.

Relation to pyelitis of pregnancy -- Pyelitis and kidney damage have been noted by many authors to occur with acute toxæmia of pregnancy. S. B. Lovelady and R. D. Mussey reviewed 117 cases of pyelitis, 92 cases occurring during pregnancy and 25 in the puerperium. In 3 of the cases occurring in pregnancy acute toxæmia accompanied or followed the disease. One other case of fulminating pyelonephritis proved fatal. Pyelitis was proved in all the cases by the presence of pus and sometimes red cells in catheter specimens of the urine. In 30 of the women pyelitis did not recur in a subsequent pregnancy. Lovelady and Mussey concluded that permanent kidney damage does not as a rule follow an attack of pyelitis, and that if the disease is treated early and properly it is not prone to cause eclampsia or pre-eclamptic toxæmia.

Treatment

Diet and hydration -- R. R. de Alvarez reports on the use of the neutral diet and hydration in the treatment of toxæmias of pregnancy. Between the years 1901 and 1938, 435 cases were studied. These were divided into two groups: those seen from 1901 to July, 1931, and those seen from July, 1931, to July, 1938. The average age in both groups was 23 years, and 63 per cent were primiparae. There were 241 cases (4.7 per cent of all deliveries) in the first group and 194 cases (6 per cent of all deliveries) in the second group. The first group was treated with general measures and observation, usually followed by termination of pregnancy in the absence of improvement. A low-protein, salt-free diet was commonly given. In the second group the hydration method was used. The patients were given abundant fluids, a neutral diet, ammonium chloride in gelatin capsules in daily doses of 8 to 12 g. with the meals, rest in bed, and mild sedation. If this method failed the pregnancy was terminated. By this method the maternal and foetal mortality-rates were about halved when compared with those of the first group.

Anterior-pituitary-like hormone -- G. van S. Smith and O. W. Smith investigated the blood and urine level of the anterior-pituitary-like hormone in 173 women suffering from late toxæmia of pregnancy. Eleven patients diagnosed as nephritic toxæmia or essential hypertension all had no rise of serum anterior-pituitary-like hormone. Of 13 women who had premature deliveries 8 had excessive amounts of the hormone in the serum. In 85 patients classed as eclamptic or pre-eclamptic 75 had high values for serum anterior-pituitary-like hormone. Twenty-seven women developed pre-eclampsia after the 7th month and 25 had a definite rise in the serum hormone 4 to 6 weeks previously. Of the 32 women whose serum values were high during the 5th, 6th, or 7th months of pregnancy none had an uneventful gestation. Twenty-five developed eclampsia and 7 had premature deliveries. In a small number of cases with a clinical diagnosis of eclampsia or pre-eclampsia the serum level was not raised. It has been found that with the rise of the anterior-pituitary-like hormone there is a decrease in the amount of progesterin and total oestrogen just at a time when they normally rise. It is therefore suggested that normal anterior pituitary hormone plays a part in the normal production of the ovarian hormones during pregnancy. It is possible that the placenta is unable to utilize the anterior pituitary hormone and the serum value therefore rises. This is accompanied by a decreased formation of progesterin and oestrogen.

- de Alvarez, R. R. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 476.
 Lovelady, S. B., and Mussey, R. D. (1940) *Proc. Mayo Clin.*, **15**, 37.
 Siddall, A. C. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 818.
 Smith, G. van S., and Smith, O. W. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 618.

Ovarian Pregnancy

Friedman Test

C. H. Davis and V. Stevens-Young report a case of ovarian pregnancy, during the first two months of which there had been two positive Friedman tests, followed by a negative test shortly before surgery was advised. The two positive tests indicated that embryonic development must have continued for at least two months.

Davis, C. H., and Stevens-Young, V. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 1063

Cervical Pregnancy

D. Desirotte demonstrated a case of cervical pregnancy, a condition which is very rare. A patient of 38 years of age who had always previously had regular menstruation, complained of irregular periods and severe loss of blood. This was so great that she had to go into hospital. Examination showed a small tumour in the uterus and a diagnosis of fibroma was suggested. Hysterectomy was performed and examination of the extirpated uterus showed the presence of a cervical pregnancy. Only a few cases have been published so far, but all authors stress the main symptom of severe loss of blood (sometimes fatal) during ablation of the placenta. Early diagnosis is therefore very important, and extirpation of the uterus necessary.

Desirotte, D. (1940) *Bruux. méd.*, **20**, 802

Tuberculosis

Tuberculin Testing during Pregnancy

C. L. Ianne and J. C. Muir report 2 cases of unsuspected tuberculosis in pregnant women with subsequent death of the infant from infection. They therefore tested 691 pregnant women with tuberculin; 284 (41 per cent) reacted positively, of which 252 were X-rayed, showing 10 cases of minimal tuberculosis, 1 moderately advanced, and 1 far advanced. Of these patients 7 were treated by pneumothorax before or immediately after delivery, 2 were treated by phrenic paralysis. From these pregnancies only 1 child has become infected with tuberculosis. Ianne and Muir recommend that the tuberculin test and X-ray examination should be carried out on all pregnant women as the early establishment of a pneumothorax enables them to carry on their pregnancy without extension of the disease. The cost of these examinations is very little more than that of the routine Wassermann reaction.

Ianne, C. L., and Muir, J. C. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 448

Clostridium welchii infections

P. B. Russell and M. J. Roach review the recorded cases of *Clostridium welchii* infections during pregnancy and report 17 cases. They divide the condition into 3 types: (i) local gas gangrene, (ii) emphysema of the uterine wall with gas in the myometrium, and (iii) gas sepsis, either general septicaemia, or metastatic gas gangrene, which are usually fatal. Many of those in the first group are mild and the patient usually recovers. In the second group death should be expected unless the affected uterine muscle can be removed. Uterine pain and circulatory collapse are the outstanding symptoms in this group. The most important method of diagnosis is by anaerobic culture of the lochia and uterine contents. X-ray examination will show early emphysema of the myometrium. Cyanosis is often present, but it must be differentiated from that due to sulphanilamide which may have been given. Jaundice may occur and other causes, such as malaria, must be excluded. Other micro-organisms cause a foul vaginal discharge and must be looked for. Gas in the lochia is pathognomonic, but usually only occurs in the last stages. The odour of the patient may be not unlike that associated with typhoid fever.

There is no specific cure. Large doses of multivalent streptococcal and *Cl. welchii* serum should be given as soon as the condition is diagnosed. The patient should be isolated and all instruments used should be fractionally sterilized. Plenty of fluids, transfusions, and repeated intrauterine douches should be given. If uterine emphy-

sema is present the part should be removed if possible. Intrauterine cultures should be taken at intervals to assess the progress of the condition. Pituitary extract may be given to help the uterus to contract.

Russell, P. B., Jr., and Roach, M. J. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 437

Pelvic Osteoarthropathy of Pregnancy

J. Young, with experience dating back for 20 years of a condition which, as he points out, was known in ancient times, described under the above title a softening of the structure of the pelvic joints, associated with increased movement. The clinical states due to joint relaxation during pregnancy (excluding coccygeal lesions) are divided into 2 main groups: (i) Symptoms confined to the sacro-iliac joints. As the symphysis pubis is not affected, the pelvis remains compact. This is a common, perhaps the chief, cause of backache in pregnancy. It is not very rare at the Antenatal Clinic of the Edinburgh Royal Maternity and Simpson Memorial Hospital 114 women, or 3 per cent, of 3,030 patients, were recognized (H. Elder). (ii) Pubo-sacro-iliac osteoarthropathy. As the pubic symphysis is affected as well as the sacro-iliac joints, each half of the pelvis can be rotated. Pain and tenderness occur in the joints. Walking is difficult and may be waddling, limping, or impossible; there may be pain and tenderness along the line of the adductor muscles of the thigh, probably due to stretching of these muscles, as during walking the side of the pelvis to which they are attached is displaced forcibly upwards. When pubic pain and symptoms are severe, it is usually possible to detect a gliding movement at the pubic symphysis if it is grasped between one finger in the vagina and the thumb over the symphysis, and the patient is asked to stand first on one foot and then on the other. The separation of the symphysis pubis can be shown radiologically as in the author's paper and by 5 figures published by I. I. Rubin. The author has seen 42 cases of this pubo-sacro-iliac osteoarthropathy among 4,512 pregnant women.

Treatment

In mild cases a strong abdomino-pelvic belt and restricted exercise may be enough to carry the patient through to delivery. In worse cases complete rest in bed for varying periods and hammock regime are necessary, and then a strong supporting belt.

Rubin, I. I. (1939) *Brit. J. Radiol.*, **12**, 649.

Young, J. (1939) *Proc. R. Soc. Med.*, **32**, 1591.

PREMATURITY

See also B. E. M. P., Vol. X, p. 126, and Surveys and Abstracts 1939, p. 493.

Treatment

Oestrin

M. B. F. Inhorn treated 14 premature infants with oestrin in an attempt to prevent loss of birth-weight and to assist a rapid return to birth-weight; 14 control premature babies were also studied. The average weight loss in the treated group was 4.3 ounces as compared with 6.9 ounces in the controls. Birth-weight was regained in 12.7 days in the treated cases and in 17 days in the untreated. The treatment consisted of 500 I.U. of an aqueous solution of oestrin (keto-hydroxyoestrin) given subcutaneously daily for the first 7 days of life. The theory underlying the treatment was that the injection supplied a stimulant which would normally reach the baby through its mother.

Inhorn, M. B. (1940) *Arch. Pediat.*, **57**, 115.

PROSTATE DISEASES

See also B. E. M. P., Vol. X, p. 146, and Surveys and Abstracts 1939, pp. 158 and 493.

Calculi

T. I. Pool and G. J. Thompson record 3 cases of prostatic calculi, between the ages of 50 and 56, in which the main symptoms were fever and chills and the

prostate was small. Usually prostatic calculi are found in conjunction with benign enlargement of the organ, or in one which has been chronically inflamed, and the symptoms are those generally ascribed to those conditions. There are 3 opinions about treatment: (i) that no patient need be operated upon for their removal; (ii) that all patients should undergo perineal section for their removal; and (iii) that in selected cases only is their removal indicated. The authors agree with the last opinion, and further believe that, when operation is necessary, it can almost always be performed by the transurethral route. In the 3 cases reported the bouts of fever and chills were ascribed to subacute prostatitis caused by the calculi which lie within infected cavities, usually drainage causes pyuria, but, if a calculus moves and obstructs the outflow, fever results.

Pool, T. L., and Thompson, G. J. (1940) *Proc. Mayo Clin.*, **15**, 77.

Simple Enlargement

Treatment

Testosterone propionate.—In a review of the male sex hormone J. S. Richardson quotes from Zuckerman and others the three main hypotheses about the causation of prostatic enlargement: (a) a lack of testicular hormone, (b) excess of testicular hormone and a lack of inhibin, and (c) an excess of oestrogen with a hormonal imbalance. After due discussion it is concluded that the testes produce oestrogenic substances, that these substances can, in animals, produce a prostatic hypertrophy closely resembling a type found in man, and that testosterone can counteract this hypertrophy. The contra-indications to the use of testosterone are (i) acute retention, (ii) chronic retention with overflow, and (iii) a small hard fibrous prostate, because it does not respond to treatment. It is added that the use of testosterone does not make operation harder, should it become necessary.

K. Merk observed the action of male sex hormones on hypertrophied prostates. He regarded this condition as an endocrine disturbance, the tumour formation being considered as only secondary. In severe cases of prostatic enlargement the action of the hormone was negligible, but its effect was remarkable in slight and medium degrees of dysuria caused by prostatic conditions. Thirty-two cases observed by the author regained their power of micturition, and their state of depression was relieved by 12 injections of 10 mg. of testosterone propionate. The author also employed the drug before and after prostatic operations.

N. J. Heckel treated 22 cases of benign prostatic hypertrophy with daily intramuscular injections of from 5 to 30 mg. of testosterone propionate. Treatment, in individual cases, lasted from 7 to 56 weeks, improvement in these cases was very slight, urinary and sexual symptoms being relieved a little in some instances. Nine of the patients were operated on by the transurethral route after the injections of the hormone. Microscopic sections of the prostatic tissue removed from these 9 patients were compared with those in untreated patients. The hormone had not any significant effect upon the histology of the prostate. The effect of the hormone upon testicular function was studied in 15 of the patients, three of whom had oligospermia before treatment was started, the hormone produced oligospermia, by action either on the anterior pituitary or the seminiferous tubules, in 10 of the other 12 patients testosterone propionate was of little use in the treatment of prostatic hypertrophy, and its prolonged use might prove harmful to testicular function.

Heckel, N. J. (1940) *J. Urol.*, **43**, 286.

Merk, K. (1939) *Z. Urol.*, **33**, 573.

Richardson, J. S. (1939) *St. Thom. Hosp. Rep.*, 2 ser., **4**, 15.

Prostatic Obstruction

Comparison of Results of Transurethral Resection and Prostatectomy

B. S. Abeshouse analyses the results from 200 consecutive cases of transurethral resections and 234 prostatectomies in the endeavour to determine the usefulness and limitations of each procedure. He concludes that transurethral resection deserves a definite place in the operative treatment of prostatic obstruction; it is the operation of choice in cases of median bar, solitary median lobe, and solitary subcervical

hypertrophies; in cases with small or moderate-sized enlargement of median or lateral lobes excellent results may be obtained. Palliative relief is obtained in carcinoma with obstructive symptoms. The method also is excellent for the removal of obstruction caused by contractions, nodules, or tags following prostatectomy and in cases of persistent suprapubic fistula. The author regards the operation as unsuitable in cases with large bi-lobe or tri-lobe hypertrophies with considerable intravesical or intra-urethral bulging. Suprapubic prostatectomy was found to be suitable for cases with marked enlargement of the prostate, especially those associated with bladder conditions requiring operation. The method does not require unusual operative skill, and ensures a good and permanent functional result. Perineal prostatectomy is the ideal operation for large hypertrophies and small fibrotic prostates with or without prostatic calculi. It is the only method offering a cure of early or concealed carcinoma. It requires greater operative skill, but when properly conducted, ensures an equally good functional result.

Abeshouse, B. S. (1939) *J. Urol.*, **42**, 1101.

Malignant Diseases

Rhabdomyosarcoma

Sarcoma of the prostate is much rarer than carcinoma less than 200 cases having been reported in the literature. Of the cases reported, not less than 19 different varieties have been described. According to Lowsley and Kimball the round-celled type comprised 30 per cent of the cases, the spindle-celled 19 per cent, myxosarcoma, leiomyosarcoma and rhabdomyosarcoma 7 per cent. The majority of these tumours have occurred in young people, the higher percentage being in the first decade. H. L. Taylor reported a case of rhabdomyosarcoma occurring in a man aged 55 years, who, at operation, was found to have a greatly enlarged prostate which could not be completely enucleated, death occurred 7 months after the onset of symptoms. Histological examination showed it to be very cellular, and composed mainly of spindle-shaped cells which, in many places were arranged in interlacing bundles. It had a fairly rich blood supply, the vessels being very thin, though haemorrhage was not marked. The majority of the cells had well-stained nuclei, which were short and thick, with rounded ends; the cytoplasm was scanty and stained poorly with eosin. There were other cells with similar nuclei, the cytoplasm of which was stained more deeply with eosin. In other areas the cells were pleomorphic.

Lowsley, O. S., and Kimball, I. N. (1934) *Brit. J. Urol.*, **6**, 328.

Taylor, H. E. (1940) *Canad. med. Ass. J.*, **42**, 120.

Treatment

Histopathological Effect of Testosterone Propionate

W. F. Keller and W. M. Hull describe the histopathological changes in the prostate following the use of testosterone propionate in 10 cases of prostatic hypertrophy and 2 cases of carcinoma of the prostate treated by R. Boland. The total dosage of testosterone employed in these cases ranged from 110 to 340 mg. In 66.66 per cent of the patients there was definite clinical improvement. Biopsies of the prostate taken before and after testosterone therapy showed the following histological changes, an apparent increased glandular proliferation, a change from cuboidal or low columnar to columnar epithelium, nuclear evidence of increased cellular activity, and a definite reduction in associated inflammation.

Keller, W. F., and Hull, W. M. (1940) *Urol. cutan. Rev.*, **44**, 18.

PSITTACOSIS

See also B. E. M. P., Vol. X, p. 175; and Surveys and Abstracts 1939, p. 496.

Clinical Picture

R. B. McMillan reports a case of psittacosis in a man, aged 69, with a history and clinical features which strongly suggested typhoid fever. This is the first case to be notified in Edinburgh and the fourth in Scotland. After enteric, dysentery, and

other causes for the fever had been excluded, psittacosis or miliary tuberculosis alone remained. The determining factor in the diagnosis was the positive complement-fixation test carried out by Professor S. P. Bedson at the London Hospital, and an interesting feature was that a further test, carried out 2 months after the illness had ceased, was as strongly positive as the original test. Unusual clinical features in this case were (i) imitation of typhoid fever by the periodic occurrence of diarrhoea, with 'pea-soup' stools, (ii) the duration of the illness being 5 weeks, as compared with the average 3 weeks for the disease, (3) the rare method of onset—an acute illness for a few days followed by an ambulatory period before the next acute stage and the development of the characteristic symptoms, and (iv) the absence of headache which is accepted as being one of the most constant features of the disease. Typical features present were the blood changes and the occurrence in the lungs of a lesion clinically resembling lobar pneumonia, but without sputum, respiratory distress, or cyanosis. A total of 20 g. of sulphapyridine, given by mouth, on the average scale of dosage recommended for pneumonia, did not produce any change in the patient's general condition, or in the lung signs.

McMillan, R. B. (1940) *Brit. med. J.*, **1**, 613.

Diagnosis

Complement-Fixation Test

K. I. Meyer and B. Eddie showed that cocto-antigens prepared from virulent mouse spleens or even more readily Rivers-I tissue cultures of the virus gave a positive complement-fixation test in human psittacosis. The test was positive as early as the 6th day after infection, and is therefore a very valuable aid to diagnosis. It may remain positive for months after the illness, probably indicating that the patient is a virus carrier. It was found that the complement binding factor and neutralizing antibodies appeared at about the same time in the blood of animals. Analysis of a few human serums showed comparable results. Convalescent serum, given intramuscularly and intravenously, was found effective against psittacosis provided it contained a large number of neutralizing antibodies.

Meyer, K. F., and Eddie, B. (1939) *J. infect. Dis.* **65**, 225.

PSORIASIS

See also B.E.M.P., Vol. X, p. 187, Cumulative Supplement, Key No. 1312; and Surveys and Abstracts 1939, p. 496.

Treatment

High Vitamin-D Dosage

G. E. Clarke administered natural fish oils in massive doses containing 300,000 to 400,000 U.S.P. units of vitamin D to 37 patients with psoriasis, daily for periods of 3 to 4 months. Calciferol in similar massive doses, was given to 107 patients with psoriasis, daily for periods of 3 to 4 months. Of the patients receiving calciferol, only 12 per cent showed complete involution of the psoriatic lesions. Of both groups 70 per cent showed no improvement.

Clarke, G. E. (1940) *Arch. Derm. Syph.*, **N**, **41**, 664.

PSYCHONEUROSES AND PSYCHOTHERAPY

See also B.E.M.P., Vol. X, p. 232, Cumulative Supplement, Key Nos. 1315-1317; Surveys and Abstracts 1939, pp. 116 and 497, and pp. 54 and 61 of this volume.

Psychoneuroses

Anxiety States

Hyperventilation.—W. Sargant described a case of the anxiety state in which the war precipitated severe symptoms. These were traced to hyperventilation induced

by excitement. The aetiology was explained to the patient and he found that, if he controlled his breathing at the onset, his symptoms were much relieved. The author pointed out that hyperventilation is quite a common response to anxiety in certain subjects. It may bring on a variety of symptoms, such as dizziness, fainting, depersonalization, physical weakness and collapse, strange sensations in the head, and hysterical outbursts, besides hyperventilation tetany. He thought that many of the cases in the last war labelled as 'disordered action of the heart (D.A.H.)' were, in reality, hyperventilation syndromes in chronically anxious or hysterical subjects. For treatment he advised relief of the anxiety, either by psychotherapy or sedation. For the hyperventilation itself symptomatic relief of an acute attack may be obtained rapidly by breathing carbon dioxide mixtures or by rebreathing into a mask or paper bag. The patient can also be instructed to hold or to regulate carefully his breathing when he experiences the onset of palpitation or anxiety. In mild cases relief may be obtained by the administration of large doses of ammonium chloride, i.e. 80 to 120 grains. Tolerance to this drug is, however, rapidly acquired.

'Shell-shock'

F. Dillon reports on the neuroses occurring among combatant troops in the war of 1914-1918. Advanced centres were established for treatment of 'shell-shock' towards the end of 1916. Apart from officers, 4,235 cases were treated up to October, 1918, of these 63.5 per cent were made fit to return to duty. The sooner the cases were dealt with the better the outlook. The following types of case were encountered: (i) A direct anxiety or fear state, characterized in the first place by general shaking. (ii) Mental confusion or stuporous phenomena. (iii) Conversion symptoms, such as mutism and paralysis, most important elements. (iv) Amnesia or fugue state as the main phenomenon. (v) Combined types in which a war neurosis developed in conjunction with an organic disorder or with a previous neurosis. These types must be differentiated in the first place from concussion, pathological fatigue states, and malingering. The average period of residence in hospital for the cases successfully treated was 18 days. Sleeplessness was cured by paraldehyde, 3 drachms. Persuasion, exhortation, and also hypnosis were generally successful.

Dillon, F. (1939) *Brit. med. J.*, **2**, 63.

Sargant, W. (1940) *Lancet*, **1**, 314.

Psychotherapy

Methodology in Psychological Medicine

E. A. Bennet considers that the development of psychological medicine in Great Britain has been accompanied by a certain feeling of inferiority followed by rivalry, even acrimonious. The reason for this is thought to be want of originality so that new ideas have been supplied from abroad. But a hopeful note is the attention recently paid to the method of attaining desired results. A distinction must be drawn between method or the general plan, and methods which are the technical and other procedures used in dealing with certain phenomena. The exclusive use of the scientific method is regarded as a remnant of the atomist psychology of the past, the conception of consciousness as a mosaic of sensations, or products of mental chemistry has been abandoned, and the form of the scientific method known as the genetic or evolutionary, has not justified the expectations formed. The scientific method is not suited for most conditions, and at present use should be made of what the author calls the individualistic method. But no one method, scientific or individualistic, is final, and they should supplement each other.

Catatonia

Treatment. J. Bieler describes a method of inducing active and voluntary movements in catatonic patients. Starting with the hypothesis that every psychotic patient retains 'a remaining link' with life, i.e. his environment with the ego-present and with the ego-past, the problem is how this remaining link is to be activated. In 3 male catatonic patients of 11, 10 and 5½ years' duration, this last remaining

link was found to be their food-seeking instinct, and, by means of the 'move-skill,' an apparatus invented by the author, the patients are stimulated to make voluntary movements in order to get food. the apparatus is somewhat on the lines of a penny in the slot machine, except that a ball, instead of a coin, has to be successfully thrown through a hole in a tall box in order to release a sweet. The results obtained show that the complete isolation of the catatonic patients from their surroundings can be avoided, and that the skill of catatonics, as measured by the move-skill apparatus, is above or at any rate equal to, that of other schizophrenic patients.

Bennet, L. A. (1940) *J. ment. Sci.*, **86**, 230

Bierer, J. (1940) *J. ment. Sci.*, **86**, 287

PSYCHOSES: AFFECTIVE PSYCHOSES

See also B.E.M.P., Vol. X, p. 267, Cumulative Supplement, Key No. 1319, and Surveys and Abstracts 1939, pp. 118 and 498

Depressive and Manic Psychoses

Treatment

Leptazol (cardiazol).—A. E. Bennett reported the results in 61 cases of depression and 9 of mania treated by leptazol (cardiazol) convulsive shock therapy. Most of the depressed patients were over the age of 45 years. Electrocardiographs showed that the convulsions did not damage the heart even in patients who already had heart disease. There were no complications in this group, though Bennett believes that leptazol convulsions lead to mechanical injuries such as fractures more often than insulin convulsions. To prevent spinal and leg fractures spinal anaesthesia was induced 1 hour before the injection was given. Injection of adrenaline immediately before the leptazol enables the same convulsion to be produced with a smaller dose and therefore subsequent nausea can be avoided in the susceptible. In patients who are apprehensive insulin coma may be induced first. At its onset the cardiazol is given and the convulsion followed by intravenous hypertonic glucose. Small doses of scopolamine 1 hour before the injection may be given instead to allay the anxiety. In this series 28 depressed patients obtained a full remission lasting from 3 to 18 months; 32 obtained a social recovery and 7 relapsed, of these seven, 4 were improved by a second course of treatment. In 57 of the patients, improvement after the treatment was rapid. An average of 6 to 7 shocks was given every 2 to 3 days for an average of 3 weeks. Four of the manic patients obtained a full remission lasting for 3 to 18 months, 4 a social remission, and 2 relapsed. One of the latter recovered subsequently and the other died of intercurrent infection. The patients received an average of 4 treatments lasting for an average of 16½ days. Bennett concluded that convulsive treatment benefits chronic depressive and manic states and is most effective in middle life and in presenile depression. He stated that it can only be used with safety in well-equipped psychiatric departments and is not suitable for home or out-patient treatment.

Bennett, A. E. (1939) *Amer. J. med. Sci.*, **198**, 695.

Depression

Treatment

Haematoporphyrin.—H. Schaeffer refers to Huhnerfeld's work as the greatest advance in the treatment of depressions. Since 1930 and 1931 when Huhnerfeld reported on 17 cases of depression, 15 of which had been improved by haematoporphyrin, a large number of papers on this subject has appeared. Haematoporphyrin is derived from haemoglobin and has a strong photo-sensitizing effect, and a stimulating action upon the organism. Depressed people, who refused food, ate without making any difficulties after they had been given haematoporphyrin. The increase in weight in these patients was, however, greater than would be expected from the increased food intake and was probably due to a direct action

upon the visceral nervous system. Haematoporphyrin has also a haematopoietic action and influences salivation and the production of sweat through the visceral nervous system. This influence upon the visceral nervous system manifests itself by modifications of the electrolytic equilibrium of the depressed persons. The calcium level of the blood falls and the potassium content increases. The urine becomes more alkaline. Most of the results obtained are highly favourable, changing according to the nature of the disease. The results are less favourable in psychoses caused by some organic disease. Strecker *et al.* find that the best results are obtained in involutional melancholia, in endogenous depressions, and in mild forms of manic-depressive psychoses. Notkin and Strimberg, however, do not observe much favourable action in their 34 cases. Huhnerfeld thinks that in Steinberg's case the dose was insufficient.

The dose must be varied according to the gravity of the symptoms and the type of disease. If taken by mouth, haematoporphyrin is given in a 5 per cent solution; for injection a 2 per cent solution is used. Huhnerfeld gives for a treatment of 40 to 60 days a total of 500 to 700 mg. In a case treated for a fortnight, Huhnerfeld gave 60 mg. by injection and 300 mg. by mouth. By mouth he uses an increasing and decreasing dose, starting with 10 drops 3 times daily increasing by 1 drop per day to 60, 80, or 100 drops per day, then progressively decreasing the dose. For injection the medium dose is 1 c.c.m. accompanied by treatment by mouth. With these doses there is no danger of phototoxic effects. The mechanism of the haematoporphyrin effect in the organism is still obscure, but it is probably connected with an influence upon the visceral nervous system.

Huhnerfeld quoted by Schaeffer.

Schaeffer, H. (1939) *Pr. méd.*, **47**, 1207.

Strecker, F. A., Palmer, H. D., and Braceland, F. I. (1937) *Amer. J. Psychiat.*, **93**, 361.

Steinberg, D. I. (1936) *Amer. J. Psychiat.*, **92**, 901.

Involuntional-Depressive Psychoses

Treatment

Modified convulsive therapy—A. W. Hackfield and C. Halvorsen described a modification of the Meduna convulsive therapy, specially suitable for treating the involuntional-depressive psychoses. This modified technique, when supplemented by intensive psychotherapy, led to 100 per cent remission in private cases, and 75 per cent in hospital cases. Apprehension common with the usual leptazol (cardiazol) technique was practically eliminated. With this method no preliminary preparation of the patient was necessary, and treatment could be given in the evening, even after the patient had eaten. In cases with pronounced depressive-stuporous states the initial dose of leptazol was 8 c.c.m., in those with marked apprehensive-agitated features it was 10 to 12 c.c.m. With this large dosage the subconvulsive reaction was eliminated. Immediately following the convulsion 3 to 4 grains of sodium amylal were given intravenously, to eliminate the post-convulsive anxiety, the uncontrolled thrashing during the post-convulsive stupor, the nausea, headache, and muscle spasm. The number of convulsion treatments given on alternate days, necessary to cause a remission, varied from 3 to 12.

Hackfield, A. W., and Halvorsen, C. (1939) *Northw. Med., Seattle*, **38**, 373.

Involuntional Melancholia

Treatment

Oestradiol benzoate—J. B. Dynes treated 7 cases of involuntional melancholia with oestradiol benzoate. The patients were given 150,000 I.U. per week in 3 equal intramuscular doses. The treatment was checked by examination of the vaginal smear, estimation of the pH of the vaginal secretions, and the stain of the vaginal mucosa with compound solutions of iodine. When these reactions showed oestrogenic activity, after about 3 to 4 weeks' treatment, the dose was dropped to 100,000 I.U. then to 50,000 I.U. per week. Vaginal smears were made every week to ascertain

the necessary maintenance dose which was as low as 10,000 to 20 000 I.U. in some cases. In 5 of the patients the mental and physical condition improved as oestrogenic activity was established and remained good on the maintenance dose. One of these patients relapsed when her treatment was discontinued. In the 2 cases in which the treatment failed there was evidence of pituitary dysfunction in one and adrenal dysfunction in the other. Dynes considered that all patients suffering from involutional melancholia should be given a fair trial with oestradiol benzoate treatment.

Dynes, J. B. (1939) *Arch. Neurol. Psychiat.*, Chicago, **42**, 248

PSYCHOSES: SCHIZOPHRENIA

See also B.E.M.P., Vol X, p 302, Cumulative Supplement, Key No 1321; Surveys and Abstracts 1939, pp 116 and 499, and p 58 of this volume

Aetiology

Hippuric-Acid Excretion

J. H. Quastel and W. T. Wales, investigating the excretion of hippuric acid after administration of sodium benzoate, had previously shown that catatonic patients as a class appeared unable to detoxicate benzoic acid at the normal rate. Carrying out similar investigations on 12 cases of catatonia the authors were able to confirm their previous work. Improvement in the ability to detoxicate benzoic acid was found in 2 catatonic patients who had improved mentally after treatment. Similar results were obtained after the intravenous injection of a solution of sodium benzoate, in 22 cases of mental disorder including 13 non-catatonic cases. Among the latter the results were varied, only 3 showing abnormally low excretion of hippuric acid. It was concluded that the lowered rate of excretion of benzoic acid among catatonic and certain other psychotic patients after oral ingestion of benzoate is not necessarily due to faulty absorption of benzoate from the bowel. The minimal normal amount of hippuric acid excreted was taken as 2.9 g.

Quastel, J. H., and Wales, W. T. (1940) *Lancet*, **1**, 402

Course and Prognosis

T. A. C. Rennie, assisted by J. B. Fowler, reports on the follow-up study of 500 schizophrenic patients seen between 1913 and 1923, of these 222 had been followed for an average of 20 years. Of the patients 42.6 per cent left the hospital well or improved and 57.34 per cent were not improved on discharge. Women stayed for an average of 2½ months in hospital and men for an average of 3½ months. The majority of the patients first became ill between the ages of 21 and 30 years. Most of those who recovered had a short stay in hospital, and the prognosis was on the whole better in women than in men. A smaller number of patients showed recovery at the end of 20 years than those who were observed for 9 years. There were 100 deaths in this series, the greatest number occurring between the ages of 21 and 30 years and most often from tuberculosis. The incidence of rehospitalization in this series varied a good deal; 33.5 per cent of the patients were never able to leave hospital, whereas 32.6 per cent were never readmitted after discharge.

Rennie, T. A. C., and Fowler, J. B. (1939) *Arch. Neurol. Psychiat.*, Chicago, **42**, 877.

Clinical Picture

Dys-Symbole

I. Skottowe describes 3 groups of cases in schizophrenia, which are generally included under the general label of schizophrenia, but can be recognized by clinical signs and are important, especially in connexion with their different reactions to shock therapy. These 3 groups are (i) the dys-symbolic, (ii) the dyskinetic, and (iii) simple paranoid thinking. Dys-symbole is defined as a state of mind which is manifested by inability to formulate conceptual thoughts upon personal topics,

or to discriminate the gradations of emotions in language intelligible to others, although the patient may be in a state of clear consciousness and is able to use words at the level of perceptual thinking, and so is not aphasic in terms of sensorimotor neurology. Dyskinesia is regarded as a disorder of motility of such a nature that the movements are fragmentary or incomplete and appear to be purposeless, although not without a conscious concomitant when considered in their environment and in relation to the content of thought. The term simple paranoid thinking is applied to cases to distinguish them from the more complex paranoid states which are really florid manifestations of dys-symbolic. The dys-symbolic patients do not reach recovery from shock treatment, whereas the dyskinetic patients react well. But dys-symbolic is predominant as regards prognosis, so that a dyskinetic patient who is also dys-symbolic is not likely to give a favourable response to shock treatment, nor is a dys-symbolic paranoid.

J. S. Thomas confirms Skottowe's conclusions in general and goes further by regarding dys-symbolic as pathognomonic of schizophrenia. He finds that it is usually not difficult to recognize dys-symbolic by its manifestations, namely thought-blocking, neologisms, bizarre delusions and hallucinations usually centred on the head or brain, or more simply by a complete inability to express thoughts on personal topics at all. As a good illustration of dys-symbolic he quotes the words of a well-known art critic that 'a lot of facts whose only claim on my interest is that they are impossible facts—arms that walk, hair made of chains, and men whose heads do develop into bird-cages. Like Desdemona, I feel that this is passing strange and wondrous pitiful'. Thomas describes the technique of elicitation of symptoms in difficult cases, in patients stuporous, mute and inaccessible. In these cases the intravenous injection of sodium amytal 7½ grains in 5 c.cm. of dissolved water is followed by a sound sleep, usually for 4 hours, and then a short phase of being a quiet, pleasantly-spoken personality.

Skottowe, I. (1939) *Proc. R. Soc. Med.*, **32**, 843.

Thomas, J. S. (1940) *J. ment. Sci.*, **86**, 100.

Treatment

Convulsion Therapy

Psychology of convulsive treatment—D. W. Abse emphasizes the importance of psychological considerations in arriving at a final explanation of the mechanism of convulsive therapy. Hughlings Jackson is credited with the dictum 'find out all about dreams, and you will then understand insanity', and now in the light of psychoanalysis this statement appeals more than it did to his contemporaries. It is suggested that the convulsion produces its effect on the psychotic patient in much the same way as noise on the dreamer, and brings the patient with a shock against reality—the convulsion being a danger-situation and its signal. An important factor is that the convulsive treatment establishes a close relation between the patient and his medical attendant, who pays much attention to the fears and difficulties of his patient and encourages him. There is not any specificity about convulsive treatment, though it is not without special indications psychological as well as physical, but the exact reaction-type, whether schizophrenic or manic-depressive, appears in itself to be unimportant as an indication. This confirms a psychological explanation along the lines of the re-establishment of the functional supremacy of the ego-complex in the personality as a result of repeated danger-situations and perceptual stimulation. Convulsive therapy should not be given to patients with a bad hereditary or pre-psychotic history, for even if temporarily benefited they are certain to relapse outside the hospital.

Leptazol (Cardiazol) Convulsive Therapy

Pathological changes—R. W. Whitehead *et al.* report on the effects of repeated convulsant doses of leptazol (cardiazol) on dogs and rabbits. Pathological changes occurred, particularly in the central nervous system, notably the cerebral cortex. Small circumscribed areas of more or less complete necrosis were found in the nervous parenchyma, and were occasionally associated with slight glial reaction, and with diffuse degeneration of moderate degree in the nerve cells. Changes

elsewhere were mild tubular degeneration in the kidneys, scattered haemorrhages in the lungs, increased amounts of haemosiderin in the spleen, and generalized visceral congestion. The fundamental factor in the pathogenesis of these lesions was regarded as vascular spasm causing insufficient blood supply and anoxaemia.

Disturbance of memory—G. Tooth and J. M. Blackburn reported defects in memory and intellectual impairment following convulsive therapy for schizophrenia, depression, and obsessional states. Memory difficulties, of the kind sometimes encountered after head injuries and in epileptics, were complained of by 9 out of 16 patients. The type of convulsant used did not appear to affect the memory and most of these patients received the same number of injections. In 5 of the cases the difficulty was still present 6 months after treatment. Intellectual capacity was lowered in 8 patients. Tooth and Blackburn concluded that the beneficial effect of these drugs, 13 cases in this group recovered and 3 were improved, outweighs the possibility of these complications arising, but they stress the fact that convulsants should not be used unless they are absolutely necessary in those whose livelihood depends upon their memory or intellectual power.

Curare for prevention of traumatic complications with leptazol therapy—A. E. Bennett employed aqueous or alcoholic extracts of crude curare for the prevention of the traumatic complications following convulsive shock therapy. For each batch of the drug employed the smallest lethal dose, per kilogram for mice was determined. The initial dose for human subjects was about one-tenth the lethal dose for mice. The drug is sterilized and injected slowly by the intravenous route, or intramuscularly. The physiological effects noted immediately after intravenous injection, and 15 minutes after intramuscular injection, are subjective heaviness of the eyelids, then bilateral ptosis, slight nystagmus, and scabismus with diplopia. There then follow rapidly weakness of the neck muscles with inability to raise the head, loss of facial expression, slow hesitant speech, and weakness of the throat and jaw muscles. Next follows weakness to complete paresis of the spinal muscles, preventing the patient from raising himself, and, lastly, complete paresis of the arms and legs. When, within 5 minutes of the intravenous injection of curare, this effect is noted, the estimated convulsant dose of leptazol (cardiazol) is given. No side-effects, except in a few cases transient urticaria, have been noted by the author, but adrenaline and prostigmin should be kept available in case respiratory failure should occur. The criterion is to employ sufficient curare to paralyse the muscles of the neck and back. The author concludes that this method adequately protects the patient from the traumatic complications of convulsive shock therapy, while the convulsions elicited by leptazol show much less tonic and clonic contraction, their therapeutic effectiveness is maintained. Further experiment is necessary before this procedure can be safely recommended for general psychiatric practice.

Compression fractures of vertebral bodies—G. Kraus and H. J. Viersma, of the Provincial Mental Hospital, Santpoort, Holland, examined radiologically 51 patients (13 males with an average age of 29, 38 females, average age 39) after undergoing von Meduna's convulsion treatment, and found 8 cases of more or less serious lesions of the spinal column. They do not expect that these injuries can be certainly prevented by precautions, such as keeping the patient during the convulsive period lying on his side, in a strongly-flexed position, lumbar anaesthesia, or mitigation of the convulsions by drugs, such as calcium gluconate, and barbiturates. The view that the convulsion treatment is comparatively harmless is condemned, and pulmonary abscess and activation of latent tuberculosis are also mentioned as sequelae, and it is suggested that Kummell's disease (thoma of nucleus pulposus) may follow. The benefit sometimes due to convulsive treatment is so remarkable that it should not be given up, but the cases should be carefully selected, and radiological examinations made before and after the treatment.

J. A. Cummins made a preliminary report on 77 cases of schizophrenia, manic-depressive psychosis, and involutional psychosis treated with leptazol (cardiazol). Of 52 cases of schizophrenia, 12 which were of less than 6 months' duration responded to treatment, 6 showing a full remission of symptoms, 4 a social remission, and 2 some improvement; of 21 which were of between 6 and 18 months' duration, 3 showed a full remission, 4 a social remission, 9 an improvement, and 5 no improvement; of 19 over 18 months' duration, none showed a full remission, 3 showed a

social remission, 4 some improvement, and 12 no improvement. The catatonic type of patient responded to leptazol therapy much better than the simple, paranoid, or hebephrenic types. The average number of convulsions required for remissions was 13, and the time in hospital for treatment about 3 months. The response to treatment in a group of 17 manic-depressives was much greater than in schizophrenics. The average number of convulsions required was 8, and the average period of treatment 2 months. The total number of patients benefiting was 12. The manic and the depressed phase of the disease responded equally well. In a group of 7 involuntary psychotics the duration of the illness, though a factor in the response to treatment, was not nearly so significant as in schizophrenia. The average number of convulsions required was 13; of the 7 patients treated, 6 benefited. One case of the psychasthenic type of psychoneurosis was treated, but showed no improvement. Of the total of 77 cases of mental illness treated, 57, or 75 per cent, benefited and were allowed out of hospital on probation. Of the other 12, 7 could go on probation, if their families were in a position to look after them.

I. Friedman *et al.* found, by X-ray investigation of the dorsal and lumbar vertebrae of 65 psychotic patients given extensive convulsive therapy, that in 11 cases single or multiple compressions of the vertebral bodies had occurred, all confined to the mid-dorsal region. None of these patients had any localizing symptoms, or any neurological or physical findings. No relation was found between the occurrence of these compressions and the number and severity of the convulsions. Predisposing factors in the form of kyphoses, ruptured disks, and even old compressions of the vertebral bodies were noted in 4 out of 13 control cases. Sudden flexor activities of the trunk musculature which predominated over simultaneous extensor movements, because of the extreme leverage of the flexor group of muscles was a precipitating factor. The already fixed flexed position of the dorsal spine accentuated by the sag of the bed during treatment seemed to cause a convergence of the intermittently acting muscle forces on the arched portion of the dorsal spine, wherein were found all the compression injuries. Employing the knee-support of the standard surgical bed as an adjustable vertebral hyperextension frame seemed to prevent the occurrence of compression injuries in a series of 16 consecutive cases.

Fractures and dislocations. Louis Carp reported the fractures and dislocations produced by muscular violence which may result from the convulsions induced by leptazol in the treatment of schizophrenia. These injuries are not produced in epileptic convulsions because the muscular violence is not so great. In 687 patients receiving the drug there were 12 with fractures and 118 with dislocations. None of the fractures was due to external violence such as falling out of bed. In 1,404 patients treated with insulin convulsions 1 showed a fracture and 2 dislocations. Fractures included those affecting the neck of the femur, the angle of the mandible, and the transverse process of the fifth lumbar vertebra. Dislocation of the mandible was the commonest dislocation. In one-third of the patients the injury occurred during the first convulsion, but other patients had had many convulsions before they sustained any injury. One author considered constitutional inferiority, malnutrition, and in some instances osteoporosis, as predisposing to injury. The injury is caused by intense spasm producing pathological incoordination between the groups of muscles. To prevent these injuries Carp suggested that forcible restraint should not be used during the convulsion, the mandible should be pressed upward to prevent its dislocation, and the arms should be held close to the trunks to prevent dislocation of the shoulder.

Blood-pressure during fit. —E. Guttman and F. Reitmann investigated the changes which occurred in the blood-pressure after an injection of leptazol and during the fit produced. They examined many patients and from an average of 15 drew a curve showing an initial rise followed by a fall during the fit and then a steep rise which, although lower, remained above the base line for a considerable time. They then observed the effect upon the blood-pressure of 6 patients of a subconvulsant dose, 3 c cm. of a 10 per cent solution. The average curve showed a maximum rise 2 minutes after injection, the height of the rise depended on the initial level. Doses nearer the convulsant threshold produce a greater rise of blood-pressure. If the blood-pressure were lowered with amyl nitrite no fit resulted from the injection of leptazol. Five experiments were carried out on 10 patients in which 10 mg. of benzedrine were given intravenously followed 1 or 2 minutes later by an injection of

leptazol 2 to 3 c.cm. below the convulsant dose. The result of these 2 injections upon the blood-pressure was the same, or even more marked, than in leptazol alone, but no fits occurred.

Prevention of fear.—W. L. Neustatter and H. Freiman stated that the unpleasant sensations, notably fear, associated with leptazol treatment for psychological illness often lead patients to decline further treatment. To obviate this they endeavoured to abolish consciousness by suitable anaesthesia before giving the injection. The convulsion obtained was just as effective and only a slight increase in the convulsant dose was necessary. Cyclopropane was found to be somewhat more desirable but not so easy to administer as nitrous oxide. Cyclopropane produces less cyanosis, probably because there is a large percentage of oxygen in the anaesthetic mixture. The leptazol should be injected just when the patient can respond to a command when under cyclopropane, but at a slightly higher level of consciousness when under nitrous oxide.

Status epilepticus as complication.—N. G. Becker and S. I. Stein reported a case of status epilepticus complicating leptazol therapy in a case of dementia praecox of the catatonic type. Within 15 seconds of administration of leptazol the patient had a typical clonic-tonic-clonic seizure of about 30 seconds' duration. A few minutes later myoclonic movements were noticed on the left side of the face, followed by another clonic-tonic-clonic convulsion. Ten minutes later another convulsion began, and there was considerable respiratory embarrassment. Sodium amylal, 7½ grains, was slowly given intravenously, and all visible signs of muscular activity disappeared. A hypertonic solution of dextrose (20 c.cm. of a 50 per cent solution) given intravenously, seemed to initiate rapid improvement.

Insulin premedication.—D. E. Sands gave 23 patients receiving leptazol or triazol for the treatment of schizophrenia premedication with insulin to reduce their resistiveness and fear. In 22 of the patients the premedication was a success. The convulsion also came on more quickly and the incidence of confusion and excitement after the convulsion was reduced. Sedatives such as morphine have been tried as premedication but they are not so good, as they often prevent a satisfactory fit after the injection of the convulsant. Ten units of insulin were given and then the dose increased by 10 units until the desired degree of co-operation was obtained.

Insulin Shock Therapy

L. C. Menzies reports on 118 cases of schizophrenia treated by insulin shock therapy. Of these 85 improved sufficiently to be sent home, 12 relapsed, and of these 6 cleared up under subsequent treatment. Of the 39 still in hospital, 12 improved and were able to work, whereas the remainder did not improve. The author recommends the intravenous method of terminating the coma, and believes that long-continued treatment is essential; he has given as many as 140 treatments before obtaining improvement.

C. Wall describes how schizophrenic patients undergoing insulin-shock therapy will, while in coma, make repeated movements. This behaviour pattern is almost always the same for the same person, thus one patient will always bite the bed-clothes and another will make sucking movements. It was noted that, as the symptoms of schizophrenia altered and the patient improved, the behaviour pattern changed. He reports 4 cases of women, the onset of whose illness was accompanied by some sexual trauma, whose symptoms became better as the behaviour pattern changed. They began with sucking or biting movements, followed by thigh-rubbing, masturbation, and finally coital movements. If there was any interruption in this series of behaviour patterns the symptoms of schizophrenia also failed to improve.

It is suggested that the symptoms were due to sexual repressions released during the coma; on the other hand the sexual manifestations may be of secondary importance. As the patient's whole personality improves under treatment, her attitude to sexual matters becomes more mature, that is, her interest finally becomes genital. Although the treatment was continued, once the sexual activities had been established there was no further improvement in the condition, and no relapse.

C. H. Roggenbau discusses the discrepancy of opinions concerning the insulin shock treatment of schizophrenia. The technique varies considerably, and should, according to the inventor Sakel, be modified according to the individual needs

of the patient. The duration of treatment varies from 6 weeks to 3 months and the dose from 300 units to a multiple of that figure.

Correct diagnosis and careful selection of schizophrenic types are very important. The outlook is good in recent cases, and in the paranoid and catatonic type of schizophrenia. These types, however, are in the author's opinion not, or not purely, schizophrenic, but caused by external influences. Pure schizophrenia (hebephrenia and 'true' catatonia) is very rarely influenced by insulin. Insulin is useful in the differential diagnosis of schizophrenia, a good response to the treatment being a sign that the patient is not suffering from genuine schizophrenia.

Intravenous insulin. P. Polatin *et al.* gave doses of 12 to 90 units of insulin to 23 patients, 19 of whom were psychotics and 4 psycho-neurotics, over a period of 2 to 13 weeks to produce rapid hypoglycaemic shock with a minimum of coma. Marked hypoglycaemic symptoms developed within 45 minutes, and spontaneous recovery generally within 2 hours. The dose of insulin was increased until rapidly developing hypoglycaemic shock occurred. With this treatment there was general improvement in the physical condition of the patients, and 48 per cent showed some degree of mental improvement. None of the patients had convulsions, nor were there any detectable injuries during treatment.

Complications—epileptiform seizures.—D. Goldman reports the incidence of epileptiform seizures in the course of 3,119 periods of hypoglycaemic shock for schizophrenia. 128 seizures were seen in 25 patients out of 65 treated in all. Convulsions appear to be a characteristic response in certain patients irrespective of the method employed. Multiple convulsions in a single shock period occurred only 3 times. Status epilepticus was not seen. Seizures occurred not only during the shock period, but also in subsequent secondary shock. The great majority of seizures occurred when coma was maximal, 2 to 4 hours after injection. The blood sugar was not, however, of value in predicting seizures. With a body temperature below 97° F. seizures are very rare. If the temperature is above 99° F. for any length of time they are likely to occur. No attempt was made to terminate the shock if a seizure occurred. Without any treatment patients invariably awaken within 10 to 20 minutes of the seizure, possibly because the seizure is accompanied by an out-pouring of adrenaline which raises the blood sugar. The arousing effect of the seizure is temporary only, and the patient later returns to coma. Seizures indicate the probable success of the treatment. Nine patients, who received metrazol after recovering from hypoglycaemia, made better recoveries than those who had spontaneous hypoglycaemic seizures. Whereas the hypoglycaemic seizure appears to be a specific response of certain patients, metrazol is not specific.

Electrically Induced Convulsions

G. W. I. H. Fleming *et al.* describe the electric convulsion treatment of schizophrenia. The technique was first worked out by Cerletti and Bini, who gave such shocks to several hundred patients without ill-effects. By the authors' method the convulsant current is switched on for only a fraction of a second and is transmitted to the cerebral cortex through large pad electrodes moistened with strong saline clamped tightly to the frontal region. A satisfactory fit is induced by 80 to 150 volts, but much larger doses are not harmful. The patient becomes immediately unconscious on the passage of the current. An epileptiform fit then follows if the current has been strong enough. After the fit the patient is inaccessible for about 10 minutes and behaves in a characteristic fashion, some patients pluck at the bed clothes, others snore loudly. Recovery is complete in 10 to 30 minutes and the patient has not any distinct memory of the shock. It is unlikely that fracture or dislocation will occur from an electrically induced fit. Five schizophrenic patients were treated by this method, 50 major and 25 minor convulsions being induced. The therapeutic results were not assessed, but the treatment was safe and easy, and did not frighten the patients. The exact mechanism of the production of the convulsions is at present unknown, but the authors consider it to be a valuable alternative treatment to cardiazol in the convulsant treatment of schizophrenia.

W. H. Shepley and J. S. McGregor (1939) describe an apparatus for inducing convulsions electrically for the treatment of mental disorders. This apparatus is essentially a modification of that devised by Bini; it consists fundamentally of two independent electrical circuits, the first is a low-voltage D.C. circuit suitable for

direct measurement of the patient's head resistance. The second is capable of applying to the electrodes an A.C. voltage which can be varied by means of a tapped auto-transformer between 50 and 150 volts. It can deliver 2,000 mA, and the time of the shock is automatically limited by an electrical time switch adjustable between 0.1 and 0.5 second. The circuit is applied at the junction of the temporal and parietal bones. The method has the advantage over drugs such as leptazol (cardiazol), in that it produces instantaneous unconsciousness and therefore fear is not produced. Although restlessness may follow the fit, no great psychomotor excitement, such as often occurs with leptazol (cardiazol), is present. Nausea and vomiting are also avoided. A typical epileptic fit lasting about 50 seconds is produced with complete restoration to consciousness in a few minutes. There is retrograde amnesia for a period of about 2 minutes before the passage of the current. The authors believe that this method will produce results as good as those obtained by drugs. It may be used to produce fits in patients while in insulin coma.

F. Golla *et al.* stated that the electrically-induced convulsion resembles closely the cardiazol fit, or a rather brief spontaneous seizure. The total duration is remarkably constant, at about 45 seconds; the tonic phase is rather shorter than in most spontaneous fits, and clonic jactitation becomes evident from the onset. From the typical character of the fit itself, and from its occasionally prolonged latency, it may be imagined that the effect of the brief, but intense and widespread, stimulus is to set up in the cortex, or possibly at a lower level, some process similar to that observed in the resting electro-encephalogram of idiopathic epileptics, a process which in favourable circumstances will throw the whole effector system into a state of rapidly alternating rest and maximal activity, a phenomenon recognized as an epileptic seizure.

F. E. Fox described 7 cases of mental illness which were treated with electrically induced convulsions, 5 cases of schizophrenia, 1 of depression, and 1 of anxiety were treated by this means. These cases were specially selected for treatment, and in every case the results were excellent. The patients were given 3 shocks a week, and it was suggested that in the physically strong more frequent treatment might give even better results. Fox summarized the advantages of this type of convulsive therapy, including the absence of fear in the patient, the absence of fractures, and the improvement in general health the treatment brings.

W. H. Shepley and J. S. McGregor (1940) show that the electrical method of producing convulsions in the treatment of schizophrenia is well tolerated by patients who are freed from the dread associated with the leptazol (cardiazol) method. Disagreeable features of drug-convulsant therapy, such as vomiting, confusion, and psycho-motor restlessness, are absent, and the method is free from complications due to former methods of technique such as thrombosis of veins. The method can be readily combined with other treatment, such as insulin, and, being a physical therapy, there are no toxic or cumulative effects. It is completely under control, a succession of unintended fits being unknown. The method is ideally suitable for indefinitely prolonged maintenance treatment in cases in which an occasional convulsion is necessary to prevent relapse. In this series of 200 induced major fits, no fractures or dislocations occurred. The method allows of ready repetition without the attendant disadvantages of a struggling patient. From the administrative point of view the method offers advantages of economy, and less nursing attention and supervision.

Glandular Extracts

S. Fischer, on the basis that there is a disturbance in the gaseous metabolism, which begins with decrease in the specific dynamic action of protein, and that the specific dynamic action of protein depends, in part at least, on secretions from the anterior lobe of the pituitary, treated 93 schizophrenic patients with anterior-pituitary-like hormones from the urine of pregnant women. An injection was given on 15 successive days; if no improvement was observed 3 or 4 weeks after the last injection, a second series of 15 injections was given. An advantage of the treatment is that it is free from danger. Of 50 patients whose psychosis had lasted for less than 6 months, 42 had a complete remission, 6 showed improvement, and 2 were not improved; of 43 patients whose psychosis had lasted more than 6 months, 17 had complete remission, 14 showed improvement, and 12 were not improved.

Nitrogen-Gas Convulsive Therapy

C. Halvorsen states that the dangers in treating psychotic patients by convulsion therapy could be decidedly reduced by inhalation of nitrogen gas. The most constant finding in the chemical convulsive treatment of the psychoses has been anoxaemia. The principle of shock, or preferably sudden production of, anoxaemia has a stimulating rebound effect on the medullary centres. The anoxia of insulin is comparatively mild. The author employed a combination of insulin and nitrogen in 7 cases, producing a total of 22 convulsive reactions with very successful results. The procedure is simple: the patient is given a coma-producing dose of insulin, and in about 2 hours myoclonic jerks occur, due to the partial asphyxia of the insulin action. At this stage pure nitrogen is administered by mask through a re-breathing bag. All the outlets of the mask are closed, no atmospheric air is admitted, and the lime filter is shut off. In 1 to 2 minutes cyanosis becomes obvious, and gradually deepens. Tonic rigidity usually begins in 4 minutes, first in the small muscles of the eye, fingers, and toes, the eyes fix straight ahead and the digits flex. During the next 30 seconds a tonic convulsion involves all the muscles of the body. The end point, used to determine maximal tonic spasm, is apnoea due to spasm of the respiratory muscles. The mask is then removed and the patient turned to the prone position, this provides drainage for saliva, if any, and prepares the patient for artificial respiration, should it be necessary.

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Mescaline Psychosis

G. T. Stockings reports the results of a series of experiments with mescaline on himself and a group of normal adults of 20 to 30 years of age to effect a comparison and correlation of the psychotic phenomena thus produced with those in the psychoses, such as schizophrenia, confusional insanity, and the manic-depressive and delusional state. Mescaline is one of the 4 active alkaloids in *Anhalonium lewinii* which grows in Mexico and Central America, and has been used from ancient times by Indians to produce a state of pleasant intoxication and visions in their religious ceremonies. The most striking effect physically in a normal subject

by the administration of mescaline is the resemblance to the appearance of a patient with an acute toxic confusional psychosis or with acute schizophrenia. The outstanding feature of the mescaline psychosis as a whole is undoubtedly the complete transformation and alteration in the psychical life of the individual, which is the common factor in all the psychotic states. The author concludes (i) that mescaline can produce in a normal person, under experimental conditions, all the phenomena present in the subjects of the psychogenic psychoses, and that this is most important as a method of elucidating the nature of mental disorders, (ii) that the psychoses are all variants of the same morbid process, due probably to a toxic amine with chemical and pharmacological properties similar to those of mescaline.

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PSYCHOSIS—ALCOHOLIC PSYCHOSIS

See also B.E.M.P., Vol. X, p. 332, and Surveys and Abstracts 1939, p. 505.

Korsakoff's Syndrome

Treatment

Vitamin B₁. K. M. Bowman *et al.* stated that, because vitamin undersaturation and vitamin deficiency are common in alcohol addicts, these may play a part in associated mental disorders. Polyneuritis is often found in this condition, pointing to a deficiency of vitamin B₁. Fifty-one patients with Korsakoff's psychosis were treated for an average of 11 days with a diet of border-line adequacy in vitamin B₁. In 6 of these patients (11.8 per cent) recovery occurred. Of the patients 36 were then given a diet rich in vitamin B₁ plus 18 g. of vegex (a yeast extract) daily for an average of 18 days. One patient (6.6 per cent) in this group recovered. Twenty-one of these patients then received 10 to 50 mg. of aneurine daily by parenteral injection for an average of 29 days. The recovery rate in this group was about 7 times as great as in those receiving the diet alone. The authors stated that it was impossible to say whether these recoveries were spontaneous or due to aneurine therapy.

Insulin-shock therapy. P. C. Talkington and T. H. Cheavens report the treatment by insulin shock in a case of Korsakoff's psychosis. The patient, a woman, aged 34, steadily went downhill in spite of 10 days' routine treatment. For accompanying peripheral neuritis she was given vitamin B₁, but without benefit. In all 53 treatments were given during 75 days, 47 satisfactory shocks being obtained. She improved from the beginning of treatment, tremor and delirium ceased during the hypoglycaemia, and after the sixth treatment these quiescent periods became longer, on the ninth day she became coherent during the hypoglycaemia. She gradually improved, gaining weight and strength, although she remained subject to hallucinations and delusions for some days. By the thirtieth day she began to get up and the peripheral neuritis was much better. After the thirty-ninth shock she was no longer suspicious, began to take an interest in her appearance, and started to work in the occupational therapy shop. After 46 treatments the peripheral neuritis was cured and she was mentally normal. She was discharged one week after treatment was stopped and, except for some amnesia over a period of 2 months, she was normal. Insulin facilitates the assimilation of glucose, the elimination of toxins, and increases the effect of sedatives in this disease. A further trial of this treatment in Korsakoff's psychosis is suggested.

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PUERPERIUM

See also B.E.M.P., Vol. X, p. 365, Cumulative Supplement, Key Nos. 1326-1329, and Surveys and Abstracts 1939, pp. 31 and 507.

Management of Normal Puerperium

After-Pains and Breast Engorgement

Testosterone propionate therapy.—A. R. Abarbanel reports on the treatment of

after-pains and painful engorgement of the breasts during the puerperium by testosterone propionate. In 25 multiparae 10 mg. of testosterone were given subcutaneously 15 minutes to 2 hours after the third stage of labour to prevent after-pains. Seventy-five women were used as controls. In the control group 24 per cent had little or no pain, and the rest were controlled by sedatives, some requiring repeated doses. In the test group 88 per cent had little or no pain and did not require sedatives. Another dose of 5 mg. of testosterone stopped the pains in 2 other cases but, in the third, no relief was obtained even after 30 mg. had been given. In 49 other patients with severe after-pains 82 per cent obtained relief from 5 mg. of testosterone intramuscularly, followed 1 hour later by 5 mg. subcutaneously. In none of the patients receiving the drug was lactation affected. The uterus was found to undergo involution more rapidly. In 44 primiparae and 6 multiparae with post-partum engorgement of the breasts, 5 mg. of testosterone propionate intramuscularly followed by 5 mg. subcutaneously brought relief in 92 per cent of cases. The drug had no effect upon lactation, and its action on the breast is not known.

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Response of Uterus to Posterior Pituitary Extracts

S. Gardiner and J. F. Bradbury investigated the responses of the human post-partum uterus to posterior pituitary extracts. They studied 200 normal patients on the sixth to ninth days after delivery. Solutions of pitocin, pitressin, and pituitrin were used. The effects of the 3 were compared on the same patient, because individual patients responded so differently to the individual drug. Except for the total duration of the effect there were no marked differences in the oxytocic effect of equivalent doses of pitocin and pitressin, proving that pitressin is oxytocic to the human uterus. Repeated intravenous injections of these substances were given and no tolerance was developed. The action of the drugs decreased, however, after repeated injection. There was no inhibition of activity in the post-partum uterus after the injections, as occurs in animals. The substances produced different actions in human subjects in many instances, notably in the oxytocic action of pitressin. This was thought to be due to the difference of species. The authors defined the human oxytocic unit as the smallest amount of posterior pituitary extract given intravenously which produced a definite effect as recorded on an intra-uterine bag on the sixth to the ninth post-partum day. They found this unit to be approximately 0.01 c.c. of either of the 3 substances.

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Complications other than Sepsis

Acute Inversion

W. B. Harer and J. A. Sharkey recorded 21 cases of acute inversion of the puerperal uterus. Of these 16 (76 per cent) were avoidable, being due to errors in technique, such as suprafundal pressure, manual removal, and traction on the cord. Five were unavoidable, 4 being spontaneous and 1 due to a short cord. Twelve (57 per cent) occurred before the placenta was detached, and 9 (43 per cent) after, 6 occurred immediately, 2 half an hour later, and one an hour later. Immediate manual replacement, together with active anti-shock treatment gave the best results (11 out of 13 cases recovered). Intermediate and delayed manual replacement, and surgical replacement, resulted in a high mortality (6 out of 7 died).

Purpura Rheumatica

J. P. Long and R. A. Orr reported a case of purpura rheumatica occurring during the puerperium. The patient was aged 22 years, and it was her second pregnancy. After her first pregnancy she had an attack of fever, which was possibly malaria. Her second pregnancy was normal except for some pain and swelling in the left ankle which was relieved with hot baths and salicylates. She had an apical systolic murmur. After 25 hours labour she was spontaneously delivered of a normal full-term infant. She bled slightly after delivery and the puerperium was normal until the fourth day when the temperature and pulse rose. Maculo-papular purpuric spots appeared on the trunk, face, and limbs. Swelling and oedema appeared

around the left ankle and the metacarpal joints. The patient was anaemic at this time, the red cell count being only 1,450,000 cells per c.mm. The platelet count was 43,500 and the spleen was enlarged 4 cm. below the costal margin. No malarial organisms were found. The coagulation time was 1 minute and the bleeding time only $2\frac{1}{2}$ minutes. The purpuric areas continued to increase in size and to coalesce. The patient was given 2 blood transfusions, 5 c.cm. of calcium gluconate solution twice a day, 5 c.cm. of haemostatic serum intramuscularly every 4 hours, and a high vitamin diet combined with yeast. Under this treatment no new spots appeared and the patient gradually recovered. Another blood transfusion was given one week after the appearance of the purpura. The red blood-cells and platelet counts rose to 3,860,000 and 159,500. The general condition continued to improve and the patient was discharged from hospital 17 days after the birth of the child. The infant was normal in every way. The cause of the purpura was thought to be a low calcium and vitamin diet during pregnancy combined with slight toxæmia.

Post-Partum Urinary Suppression

G. F. Madding *et al.* reported a case of post-partum urinary suppression, resembling bilateral cortical necrosis of the kidneys, in which recovery took place. The features of the case were: Foetal death apparently from abruptio placentae as evidenced by mild toxæmia and severe post-partum hæmorrhage from uterine atony; typical anuria, almost complete, for 8 days; clear mental condition of the patient, and freedom from symptoms except nausea and vomiting, in spite of marked nitrogen retention, and lack of any urological lesion to explain the anuria or toxæmia, other than the factor of pregnancy.

Harer, W. B., and Sharkey, J. A. (1940) *J. Amer. med. Ass.*, **114**, 2289

Long, J. P., Jnr., and Orr, R. A. (1940) *Amer. J. Obstet. Gynecol.*, **39**, 138

Madding, G. F., Binger, M. W., and Hunt, A. B. (1940) *J. Amer. med. Ass.*, **114**, 1038

Puerperal Sepsis

Ætiology

Haemolytic streptococci.—A. M. Fleming stated that more than half of the deaths from puerperal sepsis followed normal deliveries. The haemolytic streptococcus was the cause of most of these deaths, and that belonging to group A was the most frequent. Since the source of infection is in the upper respiratory tract of the patients, or more often of her attendants, Fleming examined throat-swabs of 120 female students before they started instruction in the midwifery department. Of these 22.5 per cent were carriers of haemolytic streptococci, and of these carriers only 4.2 per cent belonged to group A. There was not any evidence of any relation between the incidence in the throat of streptococci belonging to group A and the presence of tonsillar tissue. The best method of treating the condition was enforced absence from the wards and moderate exercise in the open air, rather than gargling or painting the throat. Four of the 5 students with the group A streptococcus in their throats had worked in the children's ward just before undertaking their midwifery training. The author therefore advised that this work should not be done either just before or with obstetrical work. In the last 2 years only 4 patients who developed puerperal pyrexia had haemolytic streptococci in their throats and in 2 of them the streptococcus did not belong to groups A, B, C, or G. In one case the organism belonged to group A and was identical with that found in the throats of a nurse and student in contact. In one other case the student in attendance was also found to be a carrier of haemolytic streptococci.

Treatment

Sulphanilamide.—C. A. Gordon and A. H. Rosenthal gave large doses of sulphanilamide to 118 cases of severe puerperal infections of the genital tract, regardless of their ætiology. In 45 cases (38 per cent) the clinical response was prompt and satisfactory; in 45 cases (38 per cent) the results were not convincing, yet good enough to make the authors feel that the drug might have played an important part in recovery; and in 23 cases (20 per cent) no beneficial results were noted. There were 5 deaths, a mortality of 4 per cent. In most of the cases

the drug was given according to one of the following routines, generally with an equal amount of sodium bicarbonate, for 10 or 12 days, unless discontinued for a good reason. (1) 80 grains daily for 2 days, then 40 grains daily; (2) 120 grains daily for 2 days, 80 grains daily for 3 days, and 40 grains daily thereafter, and (3) twice routine (1). The authors concluded that sulphanilamide is not indicated in mild cases of puerperal infection, but that intra-partum infections should be immediately treated with the drug. The optimal benefit may be expected from spaced maintenance doses of 20 to 30 grains of sulphanilamide and moderate fluid restriction, provided that a large initial dose has been given. In severe puerperal infections of the genital tract the drug should be employed.

T. J. Morris studied the use of sulphanilamide in puerperal and postabortal infections. He divided the cases into four types, there being 84 cases in the first group, 14 in the second, 3 in the third, and 6 in the fourth. A control series was studied in every group. The four types were, (i) when infection was limited to the uterus, vagina, or perineum, (ii) when the infection involved the pelvic cellular tissues, tubes, pelvic peritoneum, or veins; (iii) when the infection was associated with general peritonitis, and (iv) when it was associated with septicaemia. Sulphanilamide was given in doses of 90 gr. per day for at least 3 days. If the patient improved, it was then reduced to 60 gr. per day. If improvement were maintained it was reduced to 30 gr. daily and was not discontinued until the temperature was normal unless complications from its use appeared. Morris considered that the danger from toxic symptoms and complications was such that all patients should be closely observed during the treatment. Ten to 20 gr. of sodium bicarbonate was given with the drug in this series to combat any acidosis that might arise. Most of the patients were in group (i) and all the treated and control patients recovered. It was concluded that the number was not sufficient to evaluate the use of sulphanilamide in this group. In type (ii) infections there were 6 treated patients and 8 controls. One of the controls died and all treated patients survived. It was concluded that sulphanilamide reduced the number of days of fever in both type (i) and type (ii) cases, and probably prevented the infection from becoming generalized. In types (iii) and (iv) there was a larger number of control than treated cases and a larger number of controls died. It was thought that if the treatment is to be of use it must begin early and no striking results can be expected in cases of advanced infection.

Fleming, A. M. (1939) *Brit. med. J.*, **2**, 639.

Gordon, C. A., and Rosenthal, A. H. (1939) *Surg. Gynec. Obstet.*, **69**, 631.

Morris, T. J. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 67.

Inhibition of Lactation

Testosterone Propionate

J. S. Beilly and S. Solomon discussed the effect of testosterone propionate in inhibiting lactation, post-partum, in 108 cases. The dosage varied, one group of patients receiving 3 injections of 25 mg., another receiving 4 injections of 25 mg., and in a third the dosage ranged from 1 injection of 10 mg. to 5 of 25 mg. Complete inhibition of lactation was obtained in 58 per cent of the cases, partial (when milk secretion was not inhibited, but was appreciably diminished) in 40 per cent, and failure in 2 per cent. Relief from engorgement or distension and pain or discomfort in the lactating breasts was usual in the successful and partially successful groups.

S. L. Siegler and L. M. Silverstein employed testosterone propionate in 50 parturient women to inhibit lactation. The secretion of milk depends upon the activity of the hormone prolactin in the anterior pituitary gland. Testosterone is thought to act on lactation by suddenly inhibiting prolactin. The patients received 25 to 125 mg. every 12 hours intramuscularly. In 47 cases the treatment was successful. Pain and congestion disappeared in from 8 to 12 hours after giving the total dose. Cessation of lactation and involution of the breasts usually occurred about 2 days later. Three unsuccessful cases were reported in detail. No other treatment was given in this series. The hormone produced no after-pains or significant changes in bleeding in these women.

Beilly, J. S., and Solomon, S. (1940) *Endocrinology*, **26**, 236.

Siegler, S. L., and Silverstein, L. M. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 109.

PYELITIS

See also B.E.M.P., Vol. X, p. 404; Cumulative Supplement, Key Nos. 1330-1332, and Surveys and Abstracts 1939, pp. 159 and 508.

Treatment*Sulphathiazole and Sulphamethylthiazole*

H. F. Helmholtz reports on an experimental research on the bactericidal effect on the urine of sulphathiazole and sulphamethylthiazole. Both these derivatives of sulphanilamide differ from it and from sulphapyridine in exerting a bactericidal effect on *Streptococcus faecalis* and *Staphylococcus aureus*. *Staphylococcus aureus* is more susceptible than *Streptococcus faecalis* to the action of sulphathiazole, and sulphamethylthiazole is more effective than sulphathiazole in its action on *Streptococcus faecalis*. These bacteria are killed off by these drugs in a lower concentration in the urine than are the Gram-negative bacilli, of which the *Pseudomonas aeruginosa* appears to be the most resistant to the action of sulphamethylthiazole, but sulphathiazole destroys that bacterium.

T. L. Pool and F. N. Cook, from observations on 50 patients with various urinary infections, 15 being with *Escherichia coli*, 35 under sulphamethylthiazole and 15 under sulphathiazole, the usual dosage being 15 grains (1 g.) 4 times daily, confirm Helmholtz's experimental conclusions. In approximately 65 per cent of the patients the urine became sterile, this corresponds well with other reports on the treatment of urinary infections, but there is the important point that in 5 patients with *Staphylococcus aureus* infection the urine became sterile. In 7 patients with a urinary infection by *Streptococcus faecalis* the urine became sterile. It appeared that sulphathiazole and sulphamethylthiazole are less toxic than sulphanilamide and sulphapyridine. Emphasis is laid on failure of drugs to sterilize the urine in the presence of obstruction in any part of the urinary tract, a calculus, diverticulum, or tumour.

Helmholtz, H. F. (1940) *Proc. Mayo Clin.*, **15**, 65.

Pool, T. L., and Cook, F. N. (1940) *Proc. Mayo Clin.*, **15**, 113.

Pyelitis of Pregnancy*Treatment*

Sulphanilamide—G. C. Prather treated 19 women suffering from pyelitis of pregnancy with 10 grains of sulphanilamide, 4 times a day; equal doses of sodium bicarbonate were also given. Fluid intake was restricted to 3,000 c.c. per day. Eight of the patients were cured, 4 unaltered, and there was recurrence of infection in 5; 2 were not followed up. In the 4 patients not cured the urine could not be sterilized, of the 5 which recurred they developed an afebrile asymptomatic pyuria after the sulphanilamide was stopped. There were no serious toxic reactions in this group. Forty-three cases of post-partum urinary tract infection were treated by the same method. Forty-four per cent were cured, in 49 per cent the urine could not be sterilized at once, and in 7 per cent there was a recurrence from apparent cure in 7 months.

Prather, G. C. (1939) *New Engl. J. Med.*, **221**, 6.

PYLORIC OBSTRUCTION

See also B.F.M.P., Vol. X, p. 426; and Surveys and Abstracts 1939, p. 509.

Hypertrophic Stenosis of the Pylorus*Aetiology*

Primogeniture in congenital pyloric stenosis—In 221 cases of congenital stenosis of the pylorus, whose family histories were investigated by the staff of the Royal Eastern Counties Institution Research Department, 109, or 49 per cent, were first-born. In 222 cases analysed by F. A. Cockayne (1939), 126, or 58 per cent, were the results of first pregnancies. These proportions are much higher than are found for controls selected by the presence of any other disease. Among Penrose's

and Cockayne's 443 cases the incidence of consanguineous parents (6) was higher than in normal infants. Penrose suggests that the underlying cause of congenital pyloric stenosis is a recessive diathesis.

Treatment

Perlingual application of eumydrin—A Wallgren described the lingual application of eumydrin in the treatment of congenital pyloric stenosis. Atropine and papaverine have previously been used in the conservative treatment of the condition, but they may cause toxic reactions. A drop of 0.6 per cent alcoholic solution of eumydrin placed on the tongue is absorbed without causing vomiting or any toxic symptom. The dose can be repeated if necessary if vomiting does not occur. This method has been used for 12 years at Gothenberg in the treatment of pyloric stenosis with a mortality rate of only 1 per cent.

Cockayne, I. A., Personal communication, quoted by Penrose.

Penrose, I. W. (1939) *J. ment. Sci.*, **85**, 1141.

Wallgren, A. (1940) *Arch. Dis. Childh.*, **15**, 103.

PYREXIA OF OBSCURE ORIGIN

See also B I M P., Vol. X, p. 440, and Surveys and Abstracts 1939, p. 510.

Post-Operative Pyrexia

W. Townsley investigated 600 surgical cases and found that after operations there is in the majority of cases a rapid rise of temperature usually a few hours after the operation and lasting 1 to 5 days. In none of the patients had there been fever for several days before the operation. It occurred after operations for non-infective conditions. After 222 major operations there was this fever, described as marked and prolonged, in 83 per cent.; after 140 medium operations there was fever, described as small and of short duration, in 50 per cent., and after 21 minor operations there was transient fever in 14 per cent. After 78 cases of anaesthesia, fever occurred in 70 per cent. The following conclusions were drawn: (i) after surgical operation or accidental trauma an aseptic pyrexia of rapid onset and short duration follows; (ii) this is independent of anaesthesia or the type of anaesthetic; (iii) this fever depends mainly on the extent of tissue damage and effusion of blood into the tissue, and is due to toxic products of tissue breakdown, including blood, and to increased metabolic disturbance in the attempt to repair the cellular damage.

Townsley, W. (1940) *Ulster med. J.*, **9**, 14.

RADIOLOGY IN DIAGNOSIS AND TREATMENT

See also B F M P., Vol. X, p. 456, Cumulative Supplement, Key Nos. 1340-1343, Surveys and Abstracts 1939, pp. 18, 23 and 511, and pp. 94 and 98 of this volume.

Concrete as Protective Material

G. Singer *et al.* investigated the properties of concrete as a protective material against high-voltage X-rays. It was found that the lead equivalent of any concrete was an increasing function of its mass per unit area, and was independent of the nature of the mix. It was concluded that, since the protection coefficient of concrete increases rapidly with increasing excitation potential, the thickness of the concrete barrier which will provide adequate protection at, say, 400 kv. is not very much greater than that required to give the same degree of protection at a much lower voltage. With regard to samples of ordinary building blocks, a barrier about 30 cm. (11.8 in.) is adequate at 400 kv., while at about 200 kv. the thickness required is about 22 cm. (8.7 in.). With specially prepared specimens of concrete, the thickness required at 400 kv. is about 26.5 cm., and at 200 kv. is 22 cm.

Singer, G., Taylor, I. S., and Charlton, A. L. (1939) *Radiology*, **33**, 68.

Contrast Media

Intracranial Collections of Iodized Oil

I. H. Garland and F. J. Morrissey studied a group of 25 cases who had received

lipiodol injections for radiological purposes between one and 14 years previously. They found that in two-thirds of the cases traces of the oil were still scattered throughout the subarachnoid space. In none did the presence of this substance give rise to resultant symptoms, or to positive clinical neurological signs. Intracranial lipiodol tended to be immobile, but in the spinal canal, especially when present in large collections, it was freely movable. The removal of lipiodol, when a laminectomy was being performed, proved very difficult.

Per-abrodil

Poisoning.—L. P. Dolan reported a death resulting from the intravenous injection of diodrast (per-abrodil) used as a contrast medium for X-ray examination of the kidney region. After the injection of 3 c cm. the patient rapidly became cyanosed and, in spite of all emergency treatment, her heart and lungs failed and she died. It was later discovered that she had suffered from asthma, so her death was presumed to be due to allergy or anaphylaxis. To prevent another such accident Dolan took a careful history of allergy from all patients who were to receive diodrast. Tests were also made. The patient then held 2 c cm. of it in his mouth for 10 minutes. If no reaction occurred he swallowed it. Thirty minutes later allergic reactions were sought and if they were absent the drug was given intravenously in the usual way. By this method one person very sensitive to the drug was discovered and saved the possible catastrophe of its being given intravenously.

Dolan, L. P. (1940) *J. Amer. med. Ass.*, **114**, 138.

Garland, L. H., and Morrissey, L. J. (1940) *Surg. Gynec. Obstet.*, **70**, 196.

Systematic Radio-Diagnosis

Mass Radiography of Chest

P. G. Sutton considers that the most satisfactory, speedy, and economical method of mass radiological examination of the chest is X-ray screen photography. Owing to the very fast fluorescent screens now available, the improved lenses, and the increased speed of photographic films, X-ray screen photography is now a practical proposition. The use of a miniature negative enables a large number of radiographs to be taken on one strip of film, it is less expensive, and the film occupies less filing space. The films taken can be examined by a lens, or by using a projector. The cost per radiograph is small (approximately one penny). The time required is much less than for fluoroscopy.

Visualization of Heart Chambers

G. P. Robb and I. Steinberg reported their method of visualizing the chambers of the heart, the pulmonary circulation and the great blood vessels in man. Their technique consisted of (i) the rapid intravenous injection of enough radio-opaque solution, diodrast (per-abrodil) 70 per cent, to render the interior of the heart and of the thoracic blood vessels opaque to X-rays, and (ii) radiography of these structures at the time of their opacification. The method has been found to be safe and practical, and no serious by-effects resulted from 486 injections in 232 patients, many of whom were seriously ill. The usual reaction to the injection was mild and transient, and severe reactions were rare. The diodrast compound is of negligible toxicity and is excreted rapidly and completely by the kidneys. It is claimed that the method provides vital information regarding the heart, the pulmonary circulation and the great blood vessels as well as other thoracic organs, not obtainable by other means. The information obtained is of practical value in the diagnosis, prognosis, and treatment of mediastinal, heart, and lung diseases.

Gall-Bladder

Use of pitressin in cholecystography.—B. R. Kirklin and F. E. Seedorf used pitressin in a dosage of 1 c cm. (20 pressor units) given intramuscularly to eliminate intestinal gas in the study of cholecystograms. In more than 5,000 patients the number of re-examinations necessary because of flatus obscuring the view of the gall-bladder was reduced from 25 to 5 per cent or less. The authors also studied the secondary reactions produced by pitressin. In 100 patients they found no rise of blood-pressure, except slightly just after the injection. The blood-pressure slowly

dropped in this group as well as in a control group of 10 patients undergoing cholecystography but having no pitressin. The fall in blood-pressure was therefore thought to be due to rest. Many of the patients showed pallor and had nausea, belching, or intestinal cramps after receiving the pitressin. Twenty of 54 women had uterine cramps after pitressin, particularly if they had had a period less than 15 days before it was given. Pitressin caused no change in the pulse-rate in this series. Although pitressin was very useful in cholecystographic examination, the authors concluded that it was contra-indicated because of its side-effects in cardiovascular disease, old age, and pregnancy.

Kirklin, B. R., and Seedorf, I. I. (1939) *Proc. Mayo Clin.*, **14**, 502.

Robb, G. P., and Steinberg, I. (1940) *J. Amer. med. Ass.*, **114**, 474.

Sutton, P. G. (1940) *Brit. J. Tuberc.*, **34**, 55.

Radiotherapy

Roentgen Dosage in Dermatology

G. M. MacKee and A. C. Chpollaro report the roentgen equivalents experimentally obtained for erythema dose for filtered radiations commonly used in dermatology. They found that the erythema dose for filtered radiation with 137 kv and with 0.5 mm. aluminium is 400 r, with 1 mm. aluminium it is 450 r, and with 3 mm. aluminium it is 550 r. The epilating dose is between 300 and 350 r and is independent of quality, filtration, or intensity (roentgens per minute). Filtration neither improved therapeutic results nor prevented the sequelae of radiation. The half-value layer is a practical and preferable method for measuring the quality of a roentgen-ray beam. At the present time instruments of sufficient accuracy to measure X-rays of low voltage, 6 to 12 kv (Grenz rays), are not available. The authors, however, on the basis of skin effects and electrical factors for measurement of dose, estimated that the erythema dose with Grenz rays was between 200 and 300 r. Therapeutic results were no better with Grenz rays than with X-rays generally used in dermatology. Grenz rays could give rise to radio-dermatitis.

Carcinoma of Cheek

C. I. Martin describes the use of weak radium-needle treatment of carcinoma of the cheek. Calculations of the dosage showed that 7 to 8 threshold erythema doses could be delivered uniformly to intra-oral tumours by means of these needles placed parallel to one another in and around the growth, for a period of 7 days. The 10 to 13 threshold erythema doses which, in the author's opinion, were required permanently to control metastases in the cervical lymph nodes, could be given safely with a combination of weak radium-needles and divided doses of deep X-rays over a period of 7 days. In a series of 35 unselected cases of carcinoma of the mucosal portion of the cheek treated by this method, 40 per cent appeared to be well for $2\frac{1}{2}$ to 9 years.

Cancer of Cervix

New combined X-ray and radium technique—J. Z. Walker is of opinion that the failure of radium in many cases of carcinoma of the cervix uteri, when unsupported by other methods of treatment, is due to underdosage of the lateral limits of the tumour and insufficient irradiation of the intrapelvic spread. He suggests a combination of radium and X-ray therapy in which the radium is inserted in a four-cylinder vaginal applicator, the inner tubes containing two-thirds of the radium quantity of the outer cylinders. When an intra-uterine applicator is employed, the dosage from any of the radium combinations used should not exceed 28,000 r, and it is found that, if treatment is administered at fortnightly intervals, 10,000 r is a satisfactory lethal dose. When the type of applicator has been decided, the patient is put on the complementary X-ray course for this applicator, and the first half of the X-ray treatment given over 12 days. The radium application representing half the total radium dosage is given over 2 days, followed by the second half of the X-ray treatment over a further 12 days and the final radium therapy lasting a further 48 hours, the total duration of treatment representing one month. If satisfactory positioning of the radium applicator is not practicable, the complete X-ray treatment may be given before the first radium application, a procedure which is also desirable in septic cases.

Comparative Effects of Radon and Radium

Because the strength of radon seeds decreases with the length of treatment S. Russ and G. M. Scott compared the biological reactions of radium and radon on the rabbits' ovary. The initial strength of the two elements was the same, but the radon seeds were left in longer to compensate for their deterioration in strength. The effects of both the radon and radium on the ovary were almost exactly the same.

Irradiation Sickness

Treatment.—O. Lambret *et al.* investigated the blood in cases of intractable vomiting during X-irradiation. They found that, in 12 patients receiving irradiation who developed vomiting, the blood showed hyperchloraemia, especially the plasma, a fall in the alkaline reserve, an increase in pH and increased glycaemia and poly-peptidaemia. The same changes were found in 12 patients who did not vomit during irradiation. It thus appeared that vomiting was not related to the state of the body fluids. The authors found that the intravenous injection of a mixture of 75 c.c. of 30 per cent hypertonic glucose solution and 25 c.c. of 20 per cent hypertonic chloride solution, followed immediately by 15 units of insulin subcutaneously and by a further 10 units an hour later, was effective in stopping the vomiting in 75 per cent of the cases.

Vitamin B₁ therapy.—A. I. Imler and H. Wammock employed large doses of vitamin B₁ in 21 cases of irradiation sickness with good results. In most cases the subcutaneous injection of 3,000 I.U. daily gave rapid and complete relief. In a few cases recurrence of symptoms necessitated a temporary, or permanent, increase in dosage. Marked anorexia, nausea, and giddiness could generally be controlled by 3,000 I.U. daily, given by mouth, but nausea, anorexia and vomiting required 6,000 I.U. or more daily. With the oral route also relief of symptoms did not occur before 24 or 48 hours, whereas with subcutaneous injection relief occurred within 1 to 3 hours. Treatment was continued for periods varying from 3 to 20 days.

Generalized Exanthem Following

L. Loewe and M. R. Camiel reported 4 cases of a generalized exanthem, apparently associated with localized X-ray irradiation for carcinoma. The similarity of these cases was such as to suggest a distinct clinical entity with a common aetiology. All the cases had received X-rays about the neck or buccal cavity, and coincident with, or shortly after, all complained of such symptoms as soreness, pain in the mouth and sneezing with mucoid bloody discharge. On the eighth to the thirteenth day after the initial complaints an erythema of the face developed, resembling erysipelas; the mucosae of the mouth, nose and throat became involved in a membranous ulcerative process. The face lesions became vesicular, bullous, and haemorrhagic, and, six days later, crusted. Similar rashes appeared on the body, on the eighth to the seventeenth day of the illness. Coincident with the face and skin lesions the temperature rose to high levels, and fell by lysis as the rashes faded. All the patients were severely toxic, and all showed cosmophilia. Barbiturates, which had been administered at some time in each case, evidently played no important part in the development of the skin lesions.

Hypersensitivity to Sulphanilamide Following Roentgen Therapy

Photodynamic responses of patients to sulphonamide therapy following exposure to strong sunlight or ultra-violet light have been reported by many authors. M. B. Marks reported 2 cases in which hypersensitivity to sulphanilamide developed after exposure to X-rays. In one case in which hypersensitivity had developed with sulphanilamide, sulphapyridine was employed during a subsequent infection with excellent results. The author suggested that the use of X-rays concurrently with, or shortly after, sulphanilamide is contra-indicated, that, since the drug sensitizes the skin for some time after it has been discontinued, caution should be exercised as to successive repeated therapeutic light exposures; and that, when sensitivity to a sulphonamide drug exists, a change to another derivative, such as sulphapyridine, should be tried.

- Imler, A. L., and Wammock, H. (1940) *Amer. J. Roentgenol.*, **43**, 243.
 Lambret, O., Driessens, J., and Cornillot, M. (1939) *Bull. Ass. franç. Cancer*, **28**, 274.

- Loewe, L., and Camiel, M. R. (1940) *Amer. J. Roentgenol.*, **43**, 587
 MacKee, G. M., and Cipollaro, A. C. (1940) *Arch. Derm. Syph., N. Y.*, **41**, 1
 Marks, M. B. (1940) *J. Pediat.*, **16**, 503
 Martin, C. L. (1940) *Amer. J. Roentgenol.*, **43**, 226
 Russ, S., and Scott, G. M. (1940) *Lancet*, **1**, 1048
 Walker, J. Z. (1940) *Brit. J. Radiol.* NS **13**, 1

RECTUM DISEASES

See also B.F.M.P. Vol. X, p. 502 (Cumulative Supplement, Key Nos. 1346-1356 and Surveys and Abstracts 1939, p. 519)

Polypi

N. W. Swinton and S. Warren investigated polypi of the colon and rectum and their relation to malignancy in these regions. Reviewing 156 benign and malignant cases, they concluded that these polypi are true tumours and not caused by inflammation. These polypi have the same anatomical site as malignant lesions and the authors believe that they are pre-malignant. Histological examination in this series showed all variations from a benign polyp to an adeno-carcinoma. Benign polypi rarely give rise to symptoms but on becoming malignant blood and mucus appear in the stools, the bowel function alters, and abdominal pain occurs. Sex plays no part in the aetiology of polypi and they may occur at any age.

R. B. Cattell and N. W. Swinton report 10 cases of polypi in the sigmoid, 5 of which, after removal, showed early malignant change. As in all these cases bleeding was the presenting symptom, such haemorrhage of unexplained origin should suggest the presence of polypi in the sigmoid. The diagnosis depends largely on proctoscopic or sigmoidoscopic examination. After examination a barium enema should be given, and if the presence of a polyp is suspected, a double-contrast air enema will probably be necessary to demonstrate the discrete polyp, in some cases repeated X-ray examinations are necessary. These polypi should be removed by sigmoidotomy rather than by fulguration through the sigmoidoscope, because of the danger of haemorrhage, perforation and technical difficulties, and because of the difficulty of excluding cancer. Patients with large intestinal polypi should be kept under observation for an indefinite period, and sigmoidoscopic examinations and contrast enemas should be carried out annually for at least 5 years.

- Cattell, R. B., and Swinton, N. W. (1940) *New Engl. J. Med.*, **222**, 535
 Swinton, N. W., and Warren, S. (1939) *J. Amer. med. Ass.*, **113**, 1927

Benign Tumours

Rectal Tumours after Injection of Piles

R. J. Jackman reports 3 cases of the rectal tumours that may occur 1 or more years after undergoing the injection treatment of piles. The symptoms may suggest malignant disease, adenomyoma of the uterus, presacral tumours, or inflammatory conditions, such as abscess and lymphopathia venereum. Usually there are not any symptoms, but those that may occur are a feeling of fullness or incomplete defaecation, constipation, and stricture. There may be one or several nodules covered by mucosa which is often normal but may be scarred and adherent, or there may be an annular stricture. Any part of the lower half of the rectum may be involved, and the tumours may persist for 20 years after the injection. Treatment includes hot retention saline enemas and anti-constipating diet. Surgical measures are seldom necessary and may be unsatisfactory. Forceful dilatation or proctotomy for stricture is apt to give temporary relief only. On cross section the lesion is usually yellow in colour and histologically shows dense, hyaline fibrosis with numerous spaces, lymphocytes, fibroblasts, and foreign-body giant cells. According to Rosser the tumour formation is not due to phenol but to the mineral (not olive) oil in the solution injected.

- Jackman, R. J. (1940) *Proc. Mayo Clin.*, **15**, 188.
 Rosser, C. (1931) *J. Amer. med. Ass.*, **96**, 1762

Carcinoma

Treatment

Advantages of perineal colostomy—W W Babcock established a perineal colostomy in 103 cases of carcinoma of the large bowel. Although this perineal anus had no sphincter control after 3 to 4 months the patients became used to it and appreciated far more than those with an abdominal colostomy. Five per cent needed no pad or protection, as is always necessary with an abdominal colostomy, 50 per cent were able to do without a pad for most of the time by regulating the emptying of their colon and their diet. The author reported 4 cases in which an established abdominal colostomy was moved to the perineum with increased relief to the patient. He described the technique of this operation and that of establishing a perineal colostomy in the first instance in detail. The perineal colostomy has the added advantage that it is easier to palpate secondary abdominal growths if they are present.

Radiotherapy—H Chaoul describes the various types of surgical and irradiation treatment of cancer of the rectum. The best method in inoperable cancer is a combined surgical and X-ray method. The surgical measures consist in formation of an artificial anus and exposure of the tumour. The tumour is then irradiated with special near radiation tubes. The method is especially simple in cancer near the anus as no surgical exposure of the tumour is necessary, specially constructed tubes being introduced into the rectum up to the site of the tumour. The author has constructed various types of tubes to be used for the various anatomical types of cancer. For polypi he uses the normal near radiation tube (distance of anticathode 5 cm.) similar to a rectoscope; for circular and stenosing tumours a conical tube is used.

The most difficult part of the treatment is to find the correct dosage. An approximate daily dose of 500 r is recommended, with a total dose of 10,000 to 20,000 r. An indication of the adequacy of the dosage is the reduction in size of the tumour, and any dose, however large, is insufficient when this is not attained. The author has treated, since 1936, 43 patients with inoperable cancer. There was a disappearance of the tumour in 30, one of whom died from an embolus when the artificial anus was removed. Twenty-four patients are proved to be free from cancer, and in 5 patients the results are doubtful.

Babcock, W W (1939) *J. Amer. med. Ass.* **113**, 1933

Chaoul, H (1939) *Deutsch. med. Wschr.* **65**, 1149

REFLEXES IN DIAGNOSIS

See also B L M P, Vol. X, p. 558, and Surveys and Abstracts 1939, p. 520

Tendon-Jerks

Heredo-familial Tendinous Areflexia without Pupillary Changes

I. van Bogaert examined a family of 7 children, 4 of whom were normal, whereas in 3, a boy and 2 girls, tendon reflexes were absent. In another family of 8, tendon reflexes were absent in 4 girls and in a son of one of these 4. A moderate jerk was present in some individuals in whom other reflexes were absent. No other abnormality was observed in all these persons. They were free from any sign of hereditary syphilis. Necropsy was performed on one of these persons. No abnormality was observed in the central nervous system on microscopical examination. In one sciatic nerve a venous angioma and few myelinated nerve-fibres were observed. The angioma was thought to result from malformation in the venous system; it resembles the venous angiomas in the brain observed by other authors. Sporadic tendinous areflexia described in the literature belongs to 6 different groups: (i) sporadic tendinous areflexias without any associated neurological or mental symptoms, (ii) sporadic tendinous areflexias with mental symptoms, (iii) sporadic tendinous areflexia with vertebral or neural malformations, (iv) the sporadic tendinous areflexias suggestive of syphilis; (v) the so-called congenital sporadic tendinous areflexia in which another toxic or infective cause can be found, and

(vi) the areflexias noted in the course of neurological diseases which do not normally show these signs

van Bogaert, L. (1939) *J. Neurol. Psychiat.*, N S **2**, 193.

The 'Finger Reflex'

In Diagnosis of Pyramidal Tract Lesions

R. Rosner observed a reflex in the upper limbs, the 'finger reflex', which in his opinion demonstrates an affection of the pyramidal tract. Examination is made in the following way. The pronated, slightly lowered hand of the patient is kept at the wristjoint, the physician strikes with his own four fingers the volar side of the distal phalanges of the patient's four fingers. The reflex is considered to be positive if definite flexion of the thumb as well as of the four fingers arises. Whilst flexion of the four fingers may often be observed in functional cases, flexion of the thumb demonstrates organic affection of the pyramidal tract. In the majority of cases in which a positive 'finger reflex' was observed other signs, too, demonstrated organic affection. This sign is considered to be of special importance for differential diagnosis between organic and functional disease in monoparesis of an upper limb.

Rosner, R. (1940) *Schweiz. med. Wschr.*, **70**, 210.

The Bridge-of-Nose Eyelid Reflex

The bridge-of-nose eyelid reflex is a reflex of the periosteum and perichondrium. By percussion of the tip of the nose symmetrical contraction arises in the m. orbicularis oculi, so that both eyes are shut for a few moments. This reflex is always present from the age of 2 years. A Shattauer considers that it may be of value in differentiating peripheral and central facial paresis. In the presence of peripheral paresis of a facial nerve this reflex is diminished or abolished on the affected side. In central paresis it is preserved or increased. This reflex may be the only sign of former paresis of the facial nerve. Exhaustion and variability of this reflex were observed in some affections of the central nervous system, for example, in tabes dorsalis, disseminated sclerosis, and epilepsy; it was either abolished or increased. The clinical value of this reflex should certainly increase after further investigation.

Shattauer, A. (1939) *Schweiz. Arch. Neurol. Psychiat.*, **44**, 243.

REFRACTION, PRACTICAL METHODS

See also B I M P., Vol. X, p. 565, Cumulative Supplement, Key No. 1358, and Surveys and Abstracts 1939, p. 521.

Drugs Used for Production of Cycloplegia

I. S. Powell reports on the use of benzedrine sulphate as an adjuvant in cycloplegia. Four adrenergic drugs—adrenaline, benzedrine, ephedrine, and paredrine—were studied in conjunction with homatropine for the production of practical cycloplegia in young adults. The homatropine-benzedrine combination seemed most satisfactory, producing a cycloplegia as complete as homatropine but of much shorter duration. The usual homatropine cycloplegia was first studied in a group of 24 patients aged 16 to 31 years. A 2 per cent aqueous solution of homatropine hydrobromide was instilled every 5 minutes until 4 instillations had been given. Complete practical cycloplegia occurred in most cases one hour after instillation. Recovery of accommodation began in about half the cases in 8 hours; complete recovery, as judged by ability to read Jaeger 1 type, did not occur in the vast majority until after 18 hours. The pupillary size increased by an average of 4 mm., reaching its maximum half an hour after the last instillation. Diminution in the size of the pupil did not begin until the 8-hour interval and the pupils had not regained normal size at the end of 18 hours.

On studying the homatropine-benzedrine reaction a group of 100 patients was selected, aged 16 to 31 years. Two instillations of 2 per cent solution of homatropine were found to be more uniformly effective than one drop of a 5 per cent solution.

Similarly two instillations of one drop each of 1 per cent benzedrine sulphate solution produced a larger pupil and a greater clearness of the cornea than a single administration. The following technique was finally adopted. Two instillations of one drop each of 2 per cent homatropine solution were given 5 minutes apart. This was followed in 5 minutes by 2 one-drop instillations of 1 per cent benzedrine sulphate 5 minutes apart. Complete practical cycloplegia existed in 93 per cent of cases at the end of 1 hour. A beginning of the return of accommodation was evidenced by the ability to read Jaeger type at the end of 4 hours in 50 per cent of cases; at the end of 8 hours 75 per cent were able to read Jaeger 1 type and in 18 hours there was a complete return of normal accommodation in all, as measured by the Prince rule and the ability to read Jaeger 1 type. The average dilatation of the pupil was 4.5 mm.; a return to normal was evident in most cases in 4 hours and was complete in 18 hours in all cases. The adrenergic action of the benzedrine seems to have a definite clarifying action on the cornea as well as increasing the dilatation of the pupil.

The action of miotics in bringing about a return of accommodation following benzedrine-homatropine cycloplegia was studied in 24 cases and eserine solution was found the most effective. Eserine salicylate solution, buffered to a pH of 6.2 was used with advantage. One drop of a 0.5 per cent buffered solution of eserine salicylate was instilled 1½ hours after the homatropine; this brought about a practical return of accommodation in half an hour. This was followed by a moderate but definite diminution in accommodation but as the decline in the effect of the eserine progressed it was met by the natural recovery from the effects of the homatropine, so that the cycloplegia was overcome in all cases in 5½ hours following the instillation of the homatropine. The use of 1 per cent buffered eserine salicylate solution exhibited a more lasting effect than 0.5 per cent solution and all patients were able to read Jaeger 1 type at the end of 4½ hours; this stronger solution, however, produced nausea and vomiting in one patient who was given a repeated dose.

The study indicated that homatropine-benzedrine gave complete practical cycloplegia in 1 hour. There was a beginning of return of accommodation at the end of 4 hours as contrasted with homatropine alone which shows a beginning of return of accommodation in some cases only at the end of 8 hours. Eserine salicylate 0.5 per cent or 1 per cent solution will overcome homatropine-benzedrine cycloplegia and restore power of accommodation in half an hour.

Powell, L. S. (1939) *Amer. J. Ophthalm.*, **22**, 956.

RESUSCITATION

See also B.E.M.P., Vol. X, p. 596, Cumulative Supplement, Key No. 1363, and Surveys and Abstracts 1939, p. 521

Methods of Resuscitation

Atropine-Adrenaline-Strophanthin Mixture

D. Danielopolu and I. Marcou recommended a combination of cardiac massage and injection of an atropine-adrenaline-strophanthin mixture in cases of cardiac syncope. The technique is as follows. Artificial respiration is begun at once. The surgeon opens the abdomen by an incision below the diaphragm, while his assistant gives an intracardiac injection of 2 c.cm. of a solution consisting of atropine sulphate, 5 cg., adrenaline, 10 cg., strophanthin, 1 cg., and distilled water, 10 g. As soon as possible the left ventricle should be penetrated, 1 c.cm. of the solution being left therein, and the second 1 c.cm. being injected while withdrawing the needle. Immediately after the intracardiac injection, the surgeon should begin to massage the heart, through the diaphragm. A second injection of the mixture should be given after the massage. The procedure may be repeated if necessary. From time to time compression of the carotid sinus should be made.

Danielopolu, D., and Marcou, I. (1940) *Pr. méd.*, **48**, 44

RETINA DISEASES

See also B.E.M.P., Vol. X, p. 611; Cumulative Supplement, Key Nos. 1364-1379, and Surveys and Abstracts 1939, pp. 130 and 522.

Vascular Diseases*Post-Partum Obstruction of Central Retinal Artery*

Associated with hemiplegia.—A. W. W. Thomson reported a case of retinal arterial obstruction after the termination of pregnancy in a woman of 33, associated with contralateral hemiplegia, a very rare complication. The retinal change was permanent, but the hemiplegia transient. During her pregnancy she had no normal breast reaction, although this occurred in all her previous pregnancies, and for a time during a convalescence she felt the cold keenly, the symptoms being ascribed to a lesion in the pituitary. Treatment by amyl nitrite inhalation and subconjunctival injection of acetylcholine did not improve the fundus picture. In the discussion of the causation, evidence is brought to suggest that the primary lesion was in the pituitary artery and that the thrombosis spread to the central artery of the retina.

Thomson, A. W. W. (1940) *Brit. med. J.*, **1**, 387

Exudative Retinitis*Coats's Disease*

H. Ilwyn agrees that Coats's disease, or exudative retinitis, is a distinct clinical and pathological entity. The fundamental pathological element is a vascular malformation involving a definite vascular area of the retina. This malformation corresponds to telangiectasia and involves the small vessels, the terminal units, with formation of miliary aneurysms and dilatations of capillaries and veins with defective walls, which are prone to rupture. Slowing of the bloodstream in the dilated vessels and their rupture cause transudation of plasma into the retinal tissue, and haemorrhages there. The haemorrhages cause necrosis of retinal tissue, and the plasma and blood extend externally to the retina, from the plasma fibrin is deposited in the retinal tissue. The transuded plasma and the haemorrhage produce reactions consisting of the appearance of phagocytes derived from the cells of the layer of pigment epithelium and from histiocytes of the adventitia of the vessels, and the formation of fibroblasts from mesodermal elements and by metaplasia of cells from the pigment epithelium layer. The fibroblasts invade the haemorrhagic areas and cause an organization or encapsulation of these areas. When the haemorrhage is encapsulated, the central part liquefies and contains remnants of blood elements and deposits of cholesterol.

Ilwyn, H. (1940) *Arch. Ophthalm.*, N.Y., **23**, 507

RHEUMATIC INFECTION, ACUTE

See also B.E.M.P., Vol. X, p. 639; and Surveys and Abstracts 1939, pp. 135 and 523.

Aetiology*In the Tropics*

It has been stated that rheumatic fever is unknown in hot tropical regions where there is not any seasonal change of climate (L. Hill). From an investigation made at the General Hospital, Colombo, Ceylon, P. B. Fernando found that rheumatic infections amount to 2.2 per cent of the total admissions, the incidence of rheumatic carditis was 1.4 per cent of the total admissions, and 21.5 per cent of the cardiovascular admissions. A study is made of 215 patients admitted to hospital under the author's care for rheumatic infection which is an important cause of heart disease in Ceylon. The arthritic and cardiac manifestations closely resemble those in temperate regions. Mitral stenosis is the commonest valvular lesion. Subcutaneous nodules are very rare. In Singapore rheumatic fever is not rare, and among 793

necropsies in 1938 rheumatic carditis was the cause of death in 13, or 1.6 per cent (Pestana).

Fernando, P. B. (1939) *Quart J. Med. N.S.*, **8**, 261

Hill, I. (1939) *Brit. med. J.*, **2**, 276

Pestana, A. V. (1940) *Brit. med. J.*, **1**, 589

Bacteriology

W. R. F. Collis found that haemolytic streptococci could be cultured after death from many sites in patients dying of acute rheumatic fever. In 17 cases the organisms were grown from 14 out of 15 tonsils, 13 out of 27 cervical or mediastinal glands, and from 22 out of 42 heart valves. While Collis considered that the technique in the case of the glands and tonsils was good, and they could not have been contaminated from outside, he thought that it was possible that the heart valves yielded a growth of haemolytic streptococci because they were contaminated with blood which was sucked back into them at autopsy. He concluded that the bacteriological investigation of rheumatic fever would only be reliable when a completely sterile technique is mastered and applied.

Collis, W. R. F. (1939), *Lancet*, **2**, 817

Clinical Picture

Cutaneous Eruptions

H. G. Hadley summarizes the cutaneous eruptions that have been associated with acute rheumatic infection, and briefly reports 2 cases—a married woman, aged 35, presented a symmetrical elevated erythema of the anterior surfaces of both arms and a V-shaped eruption of the neck on both the anterior and posterior surfaces, fever 100° F. and general rheumatic pains. This was followed by a very severe attack of rheumatic fever with pericarditis, aortic and mitral endocarditis, a migrating form of pneumonia, and pleuritic effusion requiring paracentesis. Ten weeks later the temperature became normal for 1 week, and then the original rash with fever and multiple joint involvement recurred. Recovery eventually was good, except for the residual cardiac lesions. The other case illustrated the old belief of the association between erythema nodosum and acute rheumatism (S. Mackenzie). A girl, aged 8 years, was attacked by erythema nodosum which lasted 3 weeks without any complications or sequelae. The onset took place 2 weeks after her mother had started an attack of acute rheumatism which kept her in bed for four months with the same complications as the first case.

Antistreptolysin Titres in Sera

E. W. Todd *et al.* compared the antistreptolysin-S titres with antistreptolysin-O titres in rheumatic fever. They found the former was low and the latter high in active rheumatic fever. In rheumatic children without signs of rheumatic activity and in non-rheumatic children the antistreptolysin-S titre rises considerably on infection with the haemolytic streptococcus. If the rheumatic infection is inactive the titre rises, but not so much. If the rheumatic infection becomes active the titre falls, proportionally to the degree of activity, below that of the same child when the infection was not active. The antistreptolysin-O titre behaves in an opposite manner. It rises in children with active rheumatic fever and is highest at the height of the attack. It is also higher in rheumatic children with a haemolytic streptococcal infection than it is in the non-rheumatic.

Hadley, H. G. (1940) *Brit. J. Rheumatism*, **2**, 211, 213

Mackenzie, S. (1886) *Trans. clin. Soc. Lond.*, **19**, 215.

Todd, F. W., Coburn, A. F., and Hill, A. B. (1939) *Lancet*, **2**, 1213

Treatment

Convalescent Serum

C. A. Green *et al.* recorded the results of a preliminary investigation on the possible use of convalescent serum in the treatment of acute rheumatism. Serum was obtained from patients in good general condition about the fourth to the eighth week after the temperature had settled, who were free from all indications of cardiac

complications, and whose sedimentation rate approached normal limits. From each patient 300 to 400 c cm. of blood was obtained, the serum separated, filtered, and preserved by the addition of 0.3 per cent phenol. The serum was given either intramuscularly or intravenously in doses of 10 to 20 c cm. In some cases larger doses were given. Of 15 cases, 10 were given the serum alone, while 5 were given the serum plus other modes of treatment such as the salicylates. The serum, given in the early stages of an attack, appeared to reduce the period of pyrexia, especially in first attacks. Arthritic pain was definitely relieved in such cases. Of the 15 cases treated, 9 were considered to be benefited.

Green, C. A., Glazebrook, A. J., Thomson, S., and Hopkins, W. A.
(1940) *Proc. R. Soc. Med.*, **33**, 275

RHINOSCLEROMA

See also B F M P., Vol. X, p. 650

Treatment

Effects of Teleradiumtherapy

J. A. Weiss reviews scleroma (rhinoscleroma) in the United States and describes the histological changes following teleradiumtherapy. The disease was originally confined to Central Europe, but, in the past 45 years, 58 cases have been recorded in the United States, mainly in immigrants. It is an indolent and probably specific infective chronic granuloma of the upper air-passages and usually starts in early adult life. The probable cause is Irsch's *B. rhinoscleromatis*, which is short, Gram-negative, and encapsulated. The lesions are bilateral, usually starting in the nose, and may spread down the nasopharynx to the soft palate, uvula, faucial pillars, larynx, and trachea. The lesions are granulomatous, but rarely ulcerate. Numerous small bluish-red oedematous nodules form and slowly coalesce into cartilaginous masses. Later these atrophy into grey scars with deformities, adhesions, and stenosis. The course lasts 20–30 years. There is no pain or systemic involvement. A specific complement fixation is present in 92.5 per cent of cases. The best lines of treatment are irradiation, electrocoagulation, vaccine therapy and, if necessary, surgical measures, such as tracheotomy or laryngotomy.

The author treated one case with massive teleradiotherapy and another with excision of a nodule and teleradiotherapy. There was no recurrence. The histological changes following this irradiation are extreme fibrosis, increased hyalinization, decreased cellular content of the stroma, and disintegration and disappearance of the characteristic Mikulicz bubble cells.

Weiss, J. A. (1939) *Arch. Otolaryng.*, Chicago, **30**, 38.

RHINOSPORIDIOSIS

See also B F M P., Vol. X, p. 655, and Surveys and Abstracts 1939, p. 524

Clinical Picture

Ocular Lesions

L. W. Griffey reports a case of rhinosporidiosis in a boy of 10, involving the eye. There was a small, strawberry-coloured, nodular mass attached by a thin stalk to the upper edge of the caruncle and scleral conjunctiva. Excision of the mass and its subsequent examination revealed a dome-shaped swelling with an opaque and granular surface, which at its apex showed a dark cyst 1 mm. in diameter. The histological picture revealed chronic inflammatory tissue surrounding spores which contained hundreds of endospores.

Griffey, F. W. (1939) *Amer. J. Ophthalm.*, **22**, 1389.

RICKETS

See also B.E.M.P., Vol. X, p. 661 ; and Surveys and Abstracts 1939, pp. 38 and 524.

Treatment

Preventive

Single massive dose of calciferol.—K. Schwartzler gave all infants in his clinic, during the autumn or winter, a single dose of 15 mg. of calciferol in milk. No by-effects were observed. Most of the infants were premature births. No other prophylactic method, such as ultra-violet rays, cod-liver oil, etc., was used. Most children had a mixture of milk and citric acid with fruit juice. A number of children, to whom no prophylactic treatment was given, were used as controls and showed a. about the first year of age slight symptoms of rickets, which disappeared after actinotherapy. The children who had received the calciferol remained free from rickets.

Specific

Calciferol.—A. de G. Smith and N. A. Owens treated 13 moderate and severe cases of rickets in negro infants, 8 to 28 months of age, with a minimal dose of calciferol. Each child received 800 U.S.P. units (= 800 I.U.) during 42 days. In all the cases, except 4 severe ones, healing began at the end of the first week of treatment, and 8 of the 13 patients were almost completely cured at the end of the sixth week. The authors concluded that 800 U.S.P. units of calciferol are an adequate minimal curative dose for moderate and severe rickets in negro children.

Single massive dose of calciferol.—H. Vollmer demonstrated the harmlessness of one single massive dose of 600,000 units of vitamin D, by administering this parenterally to each of 158 children in none of whom toxic manifestations occurred. The author recommended this method for the treatment of rickets and tetany, claiming that such conditions respond to the method as promptly as to the oral administration of similar doses. After 3 to 7 days the serum calcium and phosphorus generally become normal. There is X-ray evidence of calcification within a week, and recalcification is usually complete in 30 days. Tetanic convulsions cease within 24 hours. The absorption of parenteral vitamin D depots can be accelerated by using a mixture of oil and ether as solvent, instead of oil alone.

Schwartzler, K. (1939) *Med. Klinik*, **35**, 1657

Smith, A. de G., and Owens, N. A. (1940) *J. Pediat.*, **16**, 76

Vollmer, H. (1940) *J. Pediat.*, **16**, 419

SALIVARY GLAND DISEASES

Sialoangiectasis, or Sialectasis

G. Swinburne suggested the term sialoangiectasis for a condition of the salivary glands in which the ducts and terminal ductules, and even the terminal alveoli, are dilated, resembling the dilatation of the bronchi and terminal bronchioles in bronchiectasis. The term, sialectasis, which had been used to describe the condition, is not strictly correct etymologically, being translated as 'a stretching out or dilatation of the saliva'. The author reported an unusually well-marked case in a man, aged 50. Special features of this case were the great dilatation of Stensen's and Wharton's ducts, and the dilatation of the small ductules or terminal alveoli. Another interesting feature was the fact that some years previously pernicious anaemia had developed. The author considered that the condition was probably due to inflammatory changes.

Swinburne, G. (1940) *Brit. J. Surg.*, **27**, 713

SCARLET FEVER

See also B.E.M.P., Vol. XI, p. 1, Cumulative Supplement, Key No. 1387, and Surveys and Abstracts 1939, pp. 77 and 525.

Prognosis

New Hepatic-Function Test

R. W. Carslaw suggested that the hepatic function is low in the third week in

scarlet fever, and that this has a bearing on the development of nephritis. He described a clinical test of hepatic function, employing the specific gravity of the urine and the percentage of urinary urea. The percentage of urea in the urine multiplied by 10, minus the last two figures of the specific gravity estimation of the same specimen, he called the urea factor. This factor depends on the proportion of urea in the dissolved solids in the urine. This figure was found to be normally zero. It was observed that there was a general fall in the urea factor throughout the first few weeks of the illness, and that the figure was lowest at the critical period when nephritis most commonly occurs at the end of the third week. In cases with nephritis, however, the urea factor was found to be lower than in the non-nephritic cases. The author believed that estimation of the urea factor is of value in the prognosis of scarlet fever.

Carlslaw, R. W. (1939) *Brit. med. J.*, **2**, 278

Prophylaxis

New Scarlet-Fever Antitoxin

D. B. Bradshaw immunized 658 children with a new, concentrated, and refined serum (I ederle). They were given 0.75 c.c.m. (75,000 original neutralizing units) by intramuscular injection. The serum was also used for the control of scarlet fever when it broke out in a medical or surgical ward. All children Dick-positive within 24 hours of diagnosing the primary case were given 0.75 c.c.m. of the serum and there were no secondary cases in 14 primary cases involving 135 Dick-positive contacts. The children passively immunized resisted infection when brought into contact with the haemolytic streptococcus and no cases of scarlet fever developed. 1.2 per cent in this series showed serum reactions.

Bradshaw, D. B. (1939) *Lancet*, **2**, 6

Treatment

Sulphonamide Compounds

I. C. Benn concluded that sulphanilamide was of little use in the acute febrile stages of scarlet fever, and he investigated its effect in the prevention of complications following the disease in 253 cases occurring in children under the age of 10 years. A control group was studied, both groups of children receiving the same general treatment and antiscarlatinal serum if necessary. Under the age of 2 years, 0.75 g. of sulphanilamide per 24 hours was given, from 3 to 7 years 1.5 g. and for 8 years and over, 3 g. The drug was given in 3 equal doses, and continued until the temperature had been normal for a week. If complications developed, the drug was continued as long as was indicated. No serious signs of toxæmia developed. There were no deaths in either the control or treated series. The complication-rate in the treated series was 15 per cent and that in the control series 25.3 per cent. The drug therefore appears to prevent complications. It was then given to 79 patients under 10 years of age as a prophylactic for complications, in a dosage of 1 g. daily for the first 14 days of the disease, and then again from the 21st to 28th day when patients are liable to become infected with the streptococcus by other patients since they are up and about at this time. In this group the complication-rate was only 11.4 per cent.

J. O. French discussed a series of 340 cases of scarlet fever treated under controlled conditions with sulphanilamide or benzylsulphanilamide (proseptasine), and without sulphanilamide. Treatment was carried out during the whole 4 weeks which constitutes the average period of hospitalization in the disease. The dosage of the drugs employed was large, patients of 5 years of age and over received 1 g. every 4 hours (5 g. per day) for the first 14 days, then 1 g. three times a day for a further 14 days, a total dosage of 112 g., and patients under 5 years of age received half this dosage. The results obtained showed that the drug had no significant effect in the initial symptoms of scarlet fever, or upon the kind, incidence, or duration of later complications. The author concluded that there is no justification for the use of sulphanilamide or benzylsulphanilamide in scarlet fever.

Comparative Value of Serum and Sulphonamide Compounds

M. Fox and M. Hardgrove compared the results obtained in the treatment of

scarlet fever with convalescent serum and with sulphanilamide. Of 300 hospital cases, 100 were given non-specific therapy and general cure; these patients were mild cases. To another group of 100 mild or moderately severe cases 10 grains of neoprontosil (prontosil soluble) were given twice daily for 3 days to children under 5, then 10 grains once daily for 4 days; from the 16th to the 23rd day, 10 grains were again given daily. Children over 5 were given 10 grains 3 times daily for the first 3 days, 10 grains twice daily for the next 4 days, and 10 grains twice daily from the 16th to 23rd day. To a third group of 100 patients who were moderately or severely ill, convalescent serum was given. In the serum-treated cases the temperature reached normal in a shorter time (1.7 days) than in the control cases (2.8 days) or in the neoprontosil cases (3.3 days). Cervical adenitis occurred 18 times in the control group, 8 times in the serum-treated group, and 14 times in the neoprontosil group. Otitis media occurred 12 times in the control group, 11 times in the serum group, and 8 times in the neoprontosil group. Nephritis occurred once in the serum group, and twice in each of the other groups. Arthritis occurred 4 times in the serum group and 6 times in the neoprontosil group. The total number of complications was 26 in the serum group, 32 in the neoprontosil group, and 33 in the control group. The authors concluded that neoprontosil appeared to have less effect on the initial toxicity and pyrexia of scarlet fever than did convalescent serum, but that both were useful in the treatment of the disease.

Fasting

G. Liebau states that, in a large group of children suffering from scarlet fever or diphtheria, the fasting periods, lasting 2 to 4 days, had a favourable effect on the course of these infections and on their complications and sequelae. During the fasting periods fruit juices and herbal teas were the only substances allowed, between the fasts vegetarian diets, with plenty of fruit, were given. Fever, pain, and catarrh were reduced as a result of the fasting periods, and the weight lost was quickly regained after the acute infection had subsided.

Benn, F. C. (1939) *Brit. med. J.*, **2**, 644.

Fox, M., and Hardgrove, M. (1940) *Amer. J. med. Sci.*, **199**, 495.

French, J. O. (1939) *J. Hyg., Camb.*, **39**, 581.

Liebau, G. (1939) *Munch. med. Wschr.*, **86**, 1227.

SCHILDER'S DISEASE

See also B.E.M.P., Vol. XI, p. 21.

Aetiology

I. Cardona examined the brains of two brothers who died at short intervals from Schilder's disease. Diffuse demyelination throughout the white matter was observed, especially in the centrum ovale. The process observed in these cases resulted from degeneration caused by diffuse disturbance in the lipid metabolism of the whole central nervous system. The author does not support the hypothesis that Schilder's familial disease results from generalized glial dysfunction; neither does he think that all cases of Schilder's disease result from one and the same cause. There are at least two groups of cases, one resulting from toxic inflammation and the other, especially the familial group, in which degeneration results from changes in the lipid metabolism.

Cardona, I. (1939) *Riv. Patol. nerv. ment.*, **44**, 1.

SCIATICA

See also B.E.M.P., Vol. XI, p. 26, Surveys and Abstracts 1939, p. 526.

Aetiology

Thickening of Ligamentum Flavum

W. E. Carnegie Dickson and R. J. Twort described a case in which thickening of the ligamenta flava caused low backache and sciatica. The symptoms were

essentially the same as protrusion of the intervertebral disk. Adult males are predominantly affected and there is usually a history of a fall or jerk, and both sciatica and low backache may be present. There is usually an interval between the trauma and the pain. Sensory and motor signs may be present in the legs. Sexual impotence is common. A diminished or absent ankle-jerk is the commonest objective sign. There is usually a raised total cerebrospinal fluid protein and sometimes a partial or complete block is found. Opaque myelography is essential for diagnosis. The treatment is the surgical removal of the thickened ligaments. They have to be dissected off the subjacent dura. The antero-lateral margins of the ligamenta flava form the posterior margins of the intervertebral foramina and their thickening therefore nips the emerging nerve roots. The essential lesion is an elastic contraction and thickening of the torn ligaments.

Lesions of Intervertebral Disks

J. Pennybacker stated that most ordinary cases of sciatica are due to lesions in the intervertebral disk. The lesion may be prolapse of the nucleus pulposus or herniation of the annulus fibrosis. This latter condition was present in 23 of the 30 cases reported by Pennybacker. There were 17 males and 13 females in the series and all but 5 of them had previously had some injury to the back. Pain in the back was commonly associated with the typical pain in the leg. Flattening and rigidity of the lumbar spine and lumbar scoliosis often occurred. Tenderness over the sciatic nerve and muscular weakness were often present. Operation to remove pressure on the nerve roots was undertaken in these cases with very good results. Although many cases of sciatica recover with medical treatment, Pennybacker considered it advisable to operate in those cases which do not respond to rest, in those who suffer from frequently recurring attacks, and in some chronic cases. Recurrent herniation at the site of operation is extremely rare.

Dickson, W. F. C., and Twort, R. J. (1940) *Lancet*, **1**, 1113.

Pennybacker, J. (1940) *Lancet*, **1**, 771.

Treatment

Intravenous Sodium Salts

H. B. Sutton reviewed the literature of the intravenous use of sodium salicylate and sodium iodide in rheumatism, sciatica, and lumbago. He treated 20 cases of primary sciatica by injecting intravenously 20 c.cm. of an aqueous solution containing 15 gr. of sodium salicylate and 15 gr. of sodium iodide. The injection must be given slowly or pain results at the site of the injection. All pain ceased in about 10 minutes and if it returned it did not do so for 18 hours or more. If a second injection was necessary its result was usually better than the first. In 12 cases of secondary sciatica due to some external pathological process the results were not so good. A second injection produced even less result than the first. Any effect produced in secondary sciatica is probably due to the analgesic action of sodium salicylate. In primary sciatica the action is specific as the disease is probably of 'rheumatic' origin. It was suggested that this injection might be used to differentiate the two varieties of sciatica.

Sutton, H. B. (1939) *Lancet*, **2**, 1168.

SCLERODERMIA

See also B. E. M. P., Vol. XI, p. 37; Cumulative Supplement, Key No. 1390, and Surveys and Abstracts 1939, p. 527.

Aetiology

Following Nerve Injury

K. Halter describes the case of a labourer who had, following a wound in the finger, a large thecal abscess of the left hand which necessitated extended incision. Two or three months later the patient noticed that the hand turned occasionally a livid blue colour, that he was very sensitive to cold in that hand, and that the skin of the fingers became thin and shiny. Examination showed that the operated (left) hand was colder than the other, there was no hair where the skin had become thinner.

Examination of motility and sensitivity showed an injury to the median nerve. Previous observations by various authors have shown that there is occasionally cyanosis after nerve injury and generally disturbances of the blood circulation. The cited case demonstrates the occurrence of progressive scleroderma after nerve injury and supports a nervous genesis of progressive scleroderma.

Halter, K. (1939) *Deim. Wsch.*, **109**, 1139

Treatment

X-rays

Mme. Roudinesco describes the case of a young girl who suffered from a scleroderma of the face and who was treated with X-rays. The irradiation had no effect upon the scleroderma, but a radio-dermatitis developed which subsequently healed leaving a large ugly scar. The author concludes that radiotherapy is of no avail in scleroderma, and that radiotherapy is dangerous in children and should only be used when no other treatment is satisfactory.

Roudinesco, Mme. (1940) *Bull. Soc. méd. Hôp. Paris*, **56**, 132

Oedematous Scleroderma of Hardy (Scleroedema Adultorum of Buschka)

P. A. O'Leary *et al.* analyse the clinical and pathological features of 15 patients (10 female, 5 male) between the ages of 2 and 53 years, with scleroedema adultorum. In most cases initial symptoms were heralded by acute infections, particularly those of the respiratory tract. The interval between the antecedent disease and the first appearance of oedema varied from a few days to 6 weeks. Swelling began on the neck of 12 patients, on the face of 2, and over the abdomen of one. In 6 cases the swelling spread rapidly, and became generalized, in the other cases it was confined to the upper portions of the body. Nearly always the hands and feet remained unaffected. The progress of the disease is generally complete in 2 or 3 weeks. Depending on the extent of the disease, there may be limitation of movement of the extremities, slight respiratory embarrassment, immobility of the facial expression, dysphagia and general weakness. In some reported cases the disease cleared up in a few days, whereas in others it persisted for years. Atrophy does not result. The nature of the process is still unsettled. The authors consider that, in 3 cases, the disease was materially ameliorated by removal of septic teeth or tonsils. The most valuable therapeutic results were obtained with induced fever, either alone or in conjunction with radiant heat, ultra-violet irradiation, and massage.

O'Leary, P. A., Waisman, M. and Harrison, M. W. (1940) *Amer. J. med. Sci.*, **199**, 459.

SCURVY

See also B.I.M.P., Vol. XI, p. 44, and Surveys and Abstracts 1939, p. 528

Diagnosis and Differential Diagnosis

Radiography

F. A. Park *et al.* (1935) from radiological examination concluded that an early diagnosis of scurvy in children could be made from the presence of bone defects in the distal parts of the radius and tibia. P. W. Braestrup and Sv. A. Cron repeated these observations on 25 children with a particularly low content of ascorbic acid in the blood plasma or with a history of a diet which made scurvy probable. Radiological examination of the wrists and ankles of these children did not confirm the findings of Park *et al.*

Braestrup, P. W., and Cron, Sv. A. (1939) *Acta Paediat.*, **27**, 63.

Park, F. A., Guind, H. G., Jackson, D., and Bond, M. (1935) *Arch. Dis. Childh.*, **10**, 265

SENESCENCE AND SENILITY

See also B.I. M.P., Vol. XI, p. 69; and Surveys and Abstracts 1939, p. 528.

Normal Old Age*Rarity of Centenarians*

Centenarians are very rare. R. Pearl estimated the incidence at 1 in 100,000 lives (R. Pearl), and it has been stated that they are nearly all so mediocre as to suggest the survival of the unfittest (Sarton). A family history of advanced age, supplemented by temperance and by equanimity, are important factors in their survival. Under the heading of 'Creative centenarians' Sarton has sketched the characteristics of these rare exceptions. Eugène Chevreul (1786-1889), the eminent French chemist, is the only man of science to have read a scientific paper to a society when in his 102nd year and to be president then of the *Société d'Agriculture*. Manuel Garcia (1805-1906), the musician and inventor of the laryngoscope, is the only other man of science said to have been a centenarian. B. de B. de Fontenelle (1657-1757), the French philosopher, poet, and miscellaneous writer, failed by 32 days to reach his century. The bibliophile Martin Joseph Routh (1755-1854), president of Magdalen College, Oxford, for 63 years, also nearly reached his centenary.

Pearl, R. (1931) *Hum. Biol.* **3**, 133

Sarton, G. (1940) *Bull. Hist. Med., Baltimore*, **8**, 442

Convalescence in Old Age

Lewellys Barker describes the convalescent care of old-age patients which is much neglected, especially in view of the rapid change in the ratio of the young to the old in the United States of North America. In 1930 there were 12 million children under 5 years of age and about 6½ million persons over the age of 65; unless present trends change, it seems probable that in 1975 there will not be more than 6½ million children under 5 years and there may be 30 million over 60 and perhaps 22 million persons over 65 years of age. During convalescence from diseases in later life complications involving the cardiovascular system, such as cardiac failure, paroxysmal tachycardia, thrombosis and embolism, threaten life. The convalescence from cardiac failure and coronary thrombosis must be prolonged, and occupation when resumed should at first be restricted to 1 or 2 hours in the day, and the patient be urged to cultivate a deliberate habit of life. Elderly convalescents are often very difficult to control, and, if accustomed to a full life, are prone to disdain the advice of their medical attendant, and so run the risk of sudden death or permanent invalidism. During convalescence loss of appetite, a feeling of repulsion from food and a rapid loss of weight are ominous, because senile marasmus may follow. The treatment consists in temporary separation from their families and friends and subcutaneous injection of 5 to 10 units of protamine-zinc insulin 20 minutes before breakfast and before the evening meal. Vitamin deficiency may result from the self-inflicted restrictions of diet, particularly vitamin-C deficiency, and vaginitis in old women may be due to lack of vitamin A. The old require an intake of 520 mg. calcium and 1200 mg. phosphorus daily. Hypothyroidism is not uncommon in later life; but patients with coronary disease or congestive heart failure do not tolerate thyroid treatment, even in small doses. In male patients with anxiety disturbances, hypochondriasis and depression intramuscular injection of 5 mg. in an oily solution, twice a week for 2 weeks followed by increasing doses, is said to be effective. The psychological treatment is described at some length, the elderly should 'be your age and like it'; 'lucky is the man who loving life insists upon having his clothes pressed and cleaned regularly, upon his wearing clean linen and visiting the barber and manicurist regularly'. Old people love reminiscences, and may be urged to write their autobiographies, even if they are not to be published. Family life is far better than institutional existence.

Barker, L. F. (1940) *Bull. N.Y. Acad. Med.*, 2 ser., **16**, 105

Diseases Specially Prone to Occur in Old Age

Lewellys Barker includes as diseases met with in old age and only exceptionally in early life the following: Osteoporosis, osteitis deformans, *morbus coxae senilis*, intestinal diverticula, enlarged prostate, paralysis agitans, and cerebral arteriosclerosis. There is a special tendency to suppuration of the serous membranes, the biliary tract, the genito-urinary tract, and the ear, often followed by general sepsis. The old remain free from a number of infections because immunity has been conferred by an attack in early life. To this there is a notable exception in whooping cough; for even though there was an attack in early life, the immunity may be lost. 'For this reason the grandmother should not be called into service to care for a child with whooping cough.'

Barker, I. I. (1940) *Bull. N. Y. Acad. Med.*, 2 ser., **16**, 105.

SEPTICAEMIA AND BACTERIAEMIA

See also B. F. M. P., Vol. XI, p. 76, Cumulative Supplement, Key No. 1395, and Surveys and Abstracts 1939, pp. 169 and 530.

Staphylococcal Septicaemia

Treatment

Sulphapyridine.—S. Galewski and H. S. Stannus reported a case of staphylococcal septicaemia which was successfully treated with sulphapyridine. A multiparous woman of 44 developed urinary retention due to obstruction by a large fibroid. The urine became infected with the *Staphylococcus albus* and a septicaemia followed. The patient was very ill with a high temperature and pulse-rate and neck stiffness. The cerebrospinal fluid contained albumin and cells. The patient was given sulphapyridine, 1 g., every 3 hours. Recovery was dramatic with day to day improvement, the patient receiving in all a total of 42 g.

Bacteriophage. A. B. Longacre *et al.* report on bacteriophage therapy in 36 consecutive unselected cases of septicaemia due to *Staphylococcus aureus*. An additional 54 unselected cases from hospital records were taken as a control group. The 36 cases were divided into 2 groups, (i) those treated before October, 1936, by ordinary bacteriophage, and (ii) those treated after that date by 'double potency phage'. The latter was a more potent phage which could not only clear a culture of the organism in liquid medium but also prevent subsequent growth on a blood-agar plate. The mortality in this series was: In the early group of 15 cases, 73.3 per cent and in the late group of 21 cases, 28.5 per cent, in the entire group of 36 cases, 47.2 per cent. In the control group of 54 cases, untreated by bacteriophage, the mortality was 81.4 per cent. Many of the patients treated showed metastatic abscesses. Treatment was divided into 3 parts, local, systemic or supporting, and bacteriophage. Local treatment consisted in finding and opening localized foci; in addition to drainage the wounds were irrigated daily with saline and bacteriophage. Systemic treatment was the usual supporting measure for severe infections, with transfusions in some cases. Bacteriophage was given intravenously, commencing on the first day with 0.1 c.cm. in 1 c.cm. saline, followed at hourly intervals with 0.1, 0.25, 0.5, 1, 2, 3, and 4 c.cm. respectively in 10 parts of saline. If there was physiological reaction, injections were stopped for 8 hours, and then resumed with the next smaller dose. In the absence of a reaction, 5 c.cm. were given next morning and 10 c.cm. in the afternoon. The dose was then cautiously increased by 5 c.cm. at each injection until 50 c.cm. daily had been given, or until the blood culture was negative and the temperature normal. If necessary, the dosage could be increased to 100 c.cm. per day.

Galewski, S., and Stannus, H. S. (1939) *Lancet*, **2**, 1067.

Longacre, A. B., Zaytzeff-Jern, H., and Meloney, F. L. (1940) *Surg. Gynec. Obstet.*, **70**, 1.

Streptococcal Septicaemia

Treatment

Sulphathiazole. T. S. P. Fitch described a case of *S. aureus* septicaemia success-

fully treated with sulphathiazole. The patient was a girl of 10 years, and the illness started with lumbar epidural abscess which was drained by laminectomy. The following day blood cultures were positive, and sulphathiazole therapy was started. One week later, an embolic pneumonia of the left lower lobe was detected. This was followed by an empyema which was drained by the closed method. Later still, a metastatic abscess of the right ankle developed which was also drained. In spite of large doses of sulphathiazole there was never a leucopenia, though a morbilliform and erythematous rash developed. This quickly vanished when the drug was stopped. The initial dose of the drug was 3.4 g., followed by 0.5 g. by mouth every 3 hours until 3.5 g. more were given. In the first 12 hours a total of 6.9 g., and in the following 24 hours, 3.75 g. were given. On the third day, sodium sulphathiazole intravenously in 1 g. doses (total 5 g.) was added to the oral administration. It was gradually increased until 19 g. was given in 24 hours. During the illness the patient received a total of 231.4 g. of the sulphathiazole radical, by continuous medication over a period of 17 days, an average of 13 g. per day.

Itch, T. S. P. (1940) *Arch. Pediat.*, **57**, 119.

SEX HORMONES

See also B.E.M.P., Vol. XI, p. 90; Cumulative Supplement, Key Nos. 1396-1398, Surveys and Abstracts 1939, pp. 17, 34, 108, and 531, and pp. 20, 21, 55, and 131 of this volume.

Method of Administration

Subcutaneous Implantation of Tablets

A. A. Loeser reported the results obtained from the implantation of male and female hormone tablets. In 2 cases female hormone tablets were implanted, and in 10 cases male hormone tablets. In one case in which oestradiol tablets were implanted a small infantile uterus developed so that conception occurred. Testosterone propionate tablets were implanted to control serious menorrhagia caused by fibroids, and good results were obtained in women near the menopause. General effects following implantation of testosterone were enlargement of the clitoris so long as the hormone was acting, and increased sexual drive even in older women, deepening of the voice, and temporary occurrence of lanugo, with a general feeling of well-being.

Loeser, A. A. (1940) *Brit. med. J.*, **1**, 479.

Gonadotrophic Substances

Effect of Cysteine on Gonadotrophic Hormones

H. Fraenkel-Conrat *et al.* have shown that all pituitary gonadotrophic substances, unfractionated, follicle-stimulating, and interstitial-cell-stimulating preparations, are so completely inactivated by cysteine that the minimal effective dose of the follicle-stimulating hormone became 40 times, and of the interstitial-cell-stimulating hormone more than 100 times the original level. Gonadotrophic fractions from normal male and female menopause urine (prolapsed and gadmone) were reduced by exposure to cysteine to less than 10 per cent of their original potency. On the other hand cysteine did not inactivate gonadotrophic preparations from pregnant mare serum (gonadin, gonadogen) or from human pregnancy urine (chorionic gonadotrophin, antuitrin-S). This difference in the effect of cysteine on pituitary gonadotrophic from that on placental gonadotrophic principles points to a fundamental difference in the chemical structure of these two groups of hormones.

Production of Antigonadotrophic Activity in Man

I. W. Rowlands and A. W. Spence demonstrated antigonadotrophic activity in the serum of 9 patients with undescended testes who were given daily, or twice weekly, for 12 weeks, intramuscular injections of an extract of the serum of pregnant mares. This antigonadotrophic activity developed after 4 to 6 weeks' treatment, and subsequently in most cases rose rapidly; was not proportional to the amount

of extract which was injected; generally decreased at the end of treatment, but was still present for 3 months or more (in 2 patients, however, activity increased for about 3 weeks after injections were discontinued), and was greater in patients who received twice-weekly injections of extract. No improvement in the position of the testes of the patients was observed during treatment with this extract, but, in 3 of 6 patients subsequently treated with extract of pregnancy urine, descent of the testes was successfully obtained.

Effect of Oestradiol Benzoate on Gonadotrophic Activity of Pituitary

I. W. Rowlands and I. P. Sharpey-Schafer investigated the effect of oestrogens on the gonadotrophic activity of the pituitary gland. The amount of gonadotrophin in the pituitary glands of post-menopausal women, untreated or after administration of large amounts (10 mg. or 100,000 I. U.) of oestradiol benzoate daily over periods of from 3 to 54 days was determined. It was found that the oestrogen caused a decrease in the content of gonadotrophic substance as assayed on the hypophysectomized rat. It was also shown that the presence of a small amount of a gonadotrophic substance in the urine of an ovariectomized woman was abolished by the same dose of oestradiol benzoate.

I. Raenkel-Conrat, H. Simpson, M. I., and Evans, H. M. (1939) *J. biol. Chem.*, **130**, 243.

Rowlands, I. W., and Spence, A. W. (1939) *Brit. med. J.*, **2**, 947.

— and Sharpey-Schafer, F. P. (1940) *Brit. med. J.*, **1**, 205.

Oestrogenic Substances

Effect of Prolonged Administration

B. Zondek investigated the effect of the prolonged administration of oestrogen on the uterus and anterior pituitary in the human being. Menstruation can be postponed for from 7 to 70 days by a dosage of at least 70,000 I. U. The inhibition of menstruation is caused by blocking of the gonadotrophic secretion of the anterior pituitary, whereby the development of the corpus luteum and progesterone production is prevented. As a result, the uterine mucosa cannot develop, the pre-gestational transformation is omitted, and glycogen is not produced. Larger doses (more than 600,000 I. U.) can cause glandular cystic hyperplasia. Prolonged use of very large doses (more than 600,000 I. U. for 60 days) prevents ripening of the follicle as well as corpus luteum formation, so that the ovaries appear to be those of an old woman. The cervical glands become greatly enlarged. The use of 1,400,000 I. U. of oestradiol benzoate for 28 days causes no changes in the portio; the use of 6,000,000 I. U. for 60 days caused a large, partly papillary, erosion of the portio. Even these extremely large doses did not cause carcinomatous changes in the uterus. With 6,000,000 I. U. there was a marked increase in the number of eosinophilic cells of the anterior pituitary, and an eosinophilic hyperplasia. The other endocrine glands showed no changes.

Stilboestrol

Toxic effect.—C. L. Buxton and F. T. Fingle investigated the possible toxic effects of stilboestrol in a series of 17 female patients. The dose varied from 1 mg. daily for a week to as much as 30 mg. daily for 2 to 3 weeks. Blood counts, urinalysis, serum protein partition, icteric index, and the van den Bergh reaction were investigated in all cases. The results of treatment were very good in most cases and in only one were positive toxic results found. This patient developed albuminuria with coarse and granular casts in the urine. There were no allergic reactions in this series.

Tumorigenic effect. A. Lipschutz and L. Vargas had previously shown that stilboestrol could provoke in the guinea-pig, when subjected to a prolonged treatment with subcutaneous injections of this substance, the same fibrous tumoral reaction as can the natural or esterified hormones. In a further series of experiments these findings were corroborated. This tumorigenic action of small doses of stilboestrol is much greater than that of the natural hormones (oestradiol and estrone) when equal quantities are compared. It is less than that of similar doses of esterified oestradiol, but, with greater doses, it equals that of similar doses of

certain esters of oestradiol (monobenzoate and dipropionate) The guinea-pig uterus increases beyond the normal weight more rapidly with stilboestrol than with the free natural hormones. Loss of blood from the genital tract of the guinea-pig treated with stilboestrol is more common than with the natural hormones, but as common as with similar quantities of the esterified hormones. This is considered to be a sign of a greater toxicity of stilboestrol as compared with the natural hormones.

Oestradiol Benzoate

Effect on urinary output —E. P. Sharpey-Schafer and I. Schrire investigated the effect of oestradiol benzoate on the urinary output of women before and after the menopause, of castrated women, and of men. The patients were each placed on a rigidly fixed diet of which the water and salt content was known. They were given 100,000 I.B.U. oestradiol benzoate intramuscularly daily for 10 days. Specimens of the urine were carefully collected and measured every 24 hours. In none was there any change in the urinary volume.

Properties of Stilboestrol Dipropionate and Hexoestrol

P. M. I. Bishop *et al.* investigated the properties of stilboestrol dipropionate and hexoestrol, the hydrogenated form of stilboestrol, in man. They found that these substances had oestrogenic properties similar to those of stilboestrol in so far as they were capable of inducing uterine haemorrhage in cases of amenorrhoea, relieving menopausal symptoms, effecting the appearance of cornified cells in the vaginal smear in menopausal cases, restoring to normal the condition of the vulva and vagina in senile atrophic vaginitis, relieving the pain of dysmenorrhoea, and inhibiting lactation. Moderate toxic effects occurred in 21.6 per cent of the cases treated with stilboestrol dipropionate, and in 4.5 per cent of those treated with hexoestrol.

Action of Diethylstilboestrol

R. Kurczok *et al.* investigated the effect of diethylstilboestrol in 40 gynaecological cases. The dosages ranged from 0.05 mg. to 1.0 mg. daily by mouth, and 5 mg. twice weekly by intramuscular injection. There were 15 menopausal cases, the ages ranging from 39 to 65 years. The symptoms, which consisted of the usual vasomotor disturbances and in some cases vulvar atrophy, were relieved in all cases, improvement frequently beginning 12 hours after the first dose. In 10 cases, however, treatment had to be discontinued because of persistent nausea and vomiting, in some patients 1 mg. daily was sufficient to cause constant nausea. The hormone changed the vaginal smear from that of the castrate to that of definite follicular activity. The sense of well-being generally experienced by patients taking oestrogen was completely lacking when diethylstilboestrol was taken. The remaining 25 patients had symptoms such as amenorrhoea, oligomenorrhoea, dysmenorrhoea, or genital hypoplasia. The therapeutic effects obtained with diethylstilboestrol were no different from those obtained with oestrogen, apart from unpleasant by-effects in 16 patients. The authors concluded that diethylstilboestrol possessed the same therapeutic effects as oestrogen, but that its therapeutic value was limited because of the persistent nausea and occasional vomiting which was induced in more than 50 per cent of the cases.

Clinical Uses

Method of administration —J. C. Weed *et al.* investigated the effect of stilboestrol by mouth. They found that the nausea commonly experienced could be satisfactorily controlled by giving the tablets powdered and mixed in a glass of milk. In a few cases fullness of the breasts was observed. They recommended that oestrogen therapy be individualized, that the initial dosage be at least 1 mg., three times a day, and be varied as indicated, that, when symptoms are improved, the amount be reduced to a satisfactory maintenance dose, and that the tablets be powdered and given in milk.

Stilboestrol in amenorrhoea and menopausal disorders. —F. Shorr *et al.* studied the clinical effect of the synthetic oestrogen stilboestrol on 44 women. Two of them suffered from primary amenorrhoea and the rest of them were menopausal. In

28 of the 42 menopausal women, the menopause had been artificially induced. The drug was given both orally and intramuscularly. It produced vaginal bleeding in these patients and also follicular smears. Menopause symptoms were relieved. In 80 per cent of the patients toxic reactions such as nausea, vomiting, abdominal pain, and mental changes were seen. Their severity had no relation to the size of the dose. Shorr *et al.* concluded that the oestrogenic activity of the drug was greater by mouth than that of the natural oestrogens, but, owing to the unpleasant side-effects that are often produced it should be used with great caution and only for experimental purposes.

Triphenylchloroethylene

Experiments have shown that triphenylchloroethylene will produce oestrus changes in animals. It has a very low toxicity for animals. A. I. S. Macpherson and I. M. Robertson used it clinically in the treatment of disorders in women. The drug was given either as tablets containing 200 mg., as oily injections containing 250 mg. in 5 c.c., or as pessaries, each containing 100 mg. As many as 9 tablets may be given a day without ill-effects, the injections are given once a week for 2 weeks followed by a third 2 weeks later, and the pessaries are inserted nightly for the first 14 nights, then every 2 or 3 nights, depending upon the patient's condition. In 4 cases of amenorrhoea bleeding occurred during the withdrawal time between the courses of treatment. A total dose of 12,000 to 16,000 mg. was required. Seven patients with post-menopausal vaginitis and 1 with vulvitis of possible infective origin were also treated, 4 by injection and 4 took the drug by mouth. Senile vaginitis was also present in 6. Good results were obtained in nearly all the cases and whenever the vaginal smear was taken the follicular phase was found to be present. Sixteen menopausal patients, 13 surgical and 3 physiological were all given oral treatment. They all received benefit for some time and the vaginal smear took on a sexually active character. Later, when treatment stopped, a regressive smear developed and the symptoms returned. The drug inhibited lactation in 12 patients when given by mouth and by injection. The drug acts slowly and no toxic effects are produced even after large doses. The duration of action is longer by injection, 500 mg. acts from 6 to 9 weeks. This dosage, therefore, ensures a high level of oestrogenic activity for some time.

- Bishop, P. M. F., Bowes, R. K., Boycott, M., Kellar, R., MacGregor, T. N., and Murless, B. C. (1940) *Lancet*, **1**, 629.
 Buxton, C. L., and Ingle, F. T. (1939) *J. Amer. med. Ass.*, **113**, 2318.
 Kurziock, R., Wilson, L., and Perloff, W. H. (1940) *Endocrinology*, **26**, 581.
 Lipschutz, A., and Vargas, L. (1940) *Lancet*, **1**, 541.
 Macpherson, A. I. S., and Robertson, I. M. (1939) *Lancet*, **2**, 1362.
 Sharpey-Schafer, I. P., and Schrire, I. (1939) *Lancet*, **2**, 973.
 Shorr, F., Robinson, F. H., and Papanicolaou, G. N. (1939) *J. Amer. med. Ass.*, **113**, 2312.
 Weed, J. C., Weinstein, B. B., Lock, F. R., Douglas, J. W., and Collins, C. G. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 1047.
 Zondek, B. (1940) *J. Amer. med. Ass.*, **114**, 1850.

Male Sex Hormone

Method of Assay

L. Binet and F. Luxembourg point out the possibility of using fish as test animals for endocrine substances. They use *Xiphophorus helleri* for the determination of male sex hormone in urine. The male fish has a long coloured tail-piece which serves to direct the flow of sperm into the genital orifice of the female. These fish change their sex spontaneously, the female changing into a male. It is possible to change the female *Xiphophorus* into a male by introducing testosterone propionate, giving injections twice weekly for 2 or 3 weeks of 0.05 c.c. of testosterone propionate (10 mg. per 1 c.c.). The authors injected into 17 adult female *Xiphophorus*, measuring 6 to 7 cm., an extract of male urine which had been acidified by addition of hydrochloric acid, shaken with chloroform and then with ether and dissolved in olive oil. Twelve fish had 12 intraperitoneal injections of 0.1 c.c. each (2

injections per week), 5 fish used as controls received female urine under the same conditions; 5 other fish received no treatment. Thirteen treated fish survived the experiment. After the fourth week a change in the appearance of the animals was observed. A tail-piece was formed, but no gonopode (which is formed with testosterone propionate). Of the 12 *Xiphophorus* treated with male urine, 9 survived; 8 presented clear signs of transformation but one did not. Of the 5 treated with female urine 4 survived, but showed no reaction.

Hyperaemia as a Test

I. Steinach and H. Kun stated that testosterone propionate induces hyperaemia of the scrotal region and a precocious descent of the testicles in infantile male rats. The threshold value of both these effects is 0.25 mg. A direct effect of testosterone propionate on the cutaneous circulation is indicated by the fact that hyperaemia can also be obtained in castrated animals. This effect is not produced by androsterone propionate, oestradiol benzoate, or progesterone. If this action of testosterone is specific, and this will be shown by the examination of further male-hormone compounds, the scrotal hyperaemia might be used as a test to identify testosterone. Of all the synthetic hormones investigated in these experiments, testosterone alone acted like the natural hormone.

Oestrogenic Property of Testosterone Propionate

J. F. McCahey and A. F. Rakoff injected testosterone propionate into young adult castrated female mice 7 days after ovariectomy, and found, on examining sections of the vagina, that cornification was produced, and that uterine oestrus also occurred. They thus demonstrated that the male sex-hormone also possesses an oestrogenic property. There is therefore insufficient basis for the contention that a female sex-hormone is normal to males, and that such an element may be a factor in disease.

Vasomotor Phenomena

E. P. Sharpey-Schafer reports flushes after castration in man, like the hot flushes at the menopause in women when the ovary ceases to function. These phenomena can be corrected in both sexes by treatment with the appropriate hormone. The cause of these vasomotor changes is not known, but it was found that large doses of testosterone propionate caused flushes in men and women with normally functioning sex glands. This action could be inhibited by the oestrogens. On the other hand, testosterone propionate prevents the flushes in both castrate men and women, even when massive doses are used. It is suggested that testosterone propionate acts differently depending upon whether or not the gonads are functioning; if they are not functioning, the drug inhibits some substance connected with the anterior pituitary which is normally produced in these circumstances. If the gonads are functioning, it is possible that large doses of testosterone propionate depress their activity, leading to an over-action of the anterior pituitary and therefore producing flushes.

Response of Female Organism

J. B. Hamilton and W. R. C. Golden report the results of the administration of male hormone substances to hens and newly hatched female chicks. Testosterone propionate produced a crowing response in female chicks similar to that in the male, which could not have been imitative because there was no cock to act as an example. Male characters in the female would therefore appear to be something innate which merely requires activation. The female receiving male hormones responds with male characters of the species. In the hen testosterone propionate also produced crowing of the adult male type without going through the immature stages. Androsterone also produced crowing responses in hens. The amount of crowing could not be correlated with the amount of comb growth, it seemed rather to depend upon the ability of the individual bird.

Effects on Kidneys

V. Korenchevsky and M. A. Ross investigated the effect of the sex hormones on the kidneys of rats. Gonadectomy in males, but not in females, produced 'castration' kidneys. In both normal and gonadectomized female rats and in castrated males,

the administration of male hormones produced true hypertrophy of the kidneys, and they could therefore be defined as nephrotrophic hormones. Apart from slight pathological changes produced by large doses in the kidneys of normal females, the action of testosterone esters on these organs appeared not to be harmful, but definitely beneficial, on the other hand, oestrogens in certain doses easily produced peculiar cyst-like degenerative changes in the kidneys, particularly in the boundary layer of the cortex and medulla. The authors suggested that androsterone should be clinically tested in suitable kidney diseases in males where physiological stimulation of their organs is required. It might also be tested in suitable kidney diseases in women. The application of oestrogens, however, especially in large doses, or for prolonged periods, would probably increase the pathological changes in the kidneys of women suffering from these diseases.

Androgenic Effect of Desoxycorticosterone

C. W. Hooker and V. J. Collins showed that desoxycorticosterone acetate is capable of exerting effects which are ordinarily attributed only to male sex hormone substances. Daily injections of 2 mg. into capons for 5 days resulted in an average increase of slightly more than 3 mm. in the length plus height of the combs. Daily injections of 1 mg. into castrated rats resulted in significant maintenance of the weight of the prostate and seminal vesicles, but did not prevent castration changes in the histology of these organs. Administration of 0.5 mg. and 0.25 mg. to mice had results essentially like those of the larger amounts given to rats. The androgenic activity of the compound is thus approximately 1/30 as great as that of androsterone, and the compound resembles androsterone more than testosterone in being relatively more active upon the comb than upon rodent accessories.

Clinical Uses in Men

Hypogonadism—J. F. Idelsberg and I. A. Ornstein studied the effects of the continued use of male sex hormone over a long period of time in hypogonadism in males. One patient, a man of 26 years suffering from hypogonadism and eunuchoidism, had been treated with testosterone propionate since October, 1937. The response had been good and continued. If treatment was stopped for a few days or weeks his condition always deteriorated. Mentally and physically he was now definitely masculine and had received in all 2,000 mg. of the drug. His minimal maintenance dose was about 50 to 60 mg. a week. There have been no ill-effects from the treatment. Three other similar cases were reported with equally good results. In one case, associated with undescended testicles, the patient was after a time able to do without his maintenance dose. The patients could be taught to give their own injections as a diabetic gives himself insulin. Young patients responded better than older ones, i.e., those over about 30 years of age.

J. E. Howard and S. A. Vest reported the results of the use of testosterone propionate in sesame oil in 22 adult patients with hypogonadism. Development or re-establishment of secondary sexual characteristics with induction of normal libido and potentia was observed. The dosage for maintenance and optimal therapy was generally 25 mg. given hypodermically, twice a week. Smaller doses, if given more frequently, seemed equally effective.

Mental disorders—A. Guidham reported 4 cases of mental disorder treated with male sex hormones. The first patient was a man of 53 years suffering from an anxiety state with obsessional features. He developed marked paranoid symptoms. He was given testoviron (testosterone propionate) 5 mg. daily, intramuscularly for 20 days. His mental and physical condition rapidly improved, and 6 weeks later he was discharged from hospital no longer paranoid. A man of 26 years with obsessional tendencies and early signs of schizophrenia was given the same treatment as the first patient, for 23 days. He improved greatly and 5½ weeks later was able to enter the army for 2 months' training. Two other cases, one of senile melancholia and the other of psychoneurosis, were similarly treated with testoviron or proviron (andriosterone). Both improved sufficiently to return to normal social life and work afterwards. The author believed that male sex hormone therapy acts because psychological factors depend upon the state of the vegetative nervous system, which in turn depends upon the state of the glands.

Clinical Uses in Women

Biological effects—S. H. Geist *et al.* studied the effects of testosterone propionate

in a series of 25 women with normal menstrual cycles. Endometrial biopsies were made, and vaginal smears taken before, during, and after administration. It was found that testosterone propionate in doses of 500 mg. or more, per month produced a temporary suppression of menstruation, hypoplasia or atrophy of the endometrium, and evidence of oestrogen deficiency in the vaginal smear. In all cases a return to normal occurred after cessation of treatment. With doses of 200 mg. or less, per month, menstruation was not suppressed, nor were there any demonstrable changes in the vaginal smear. Doses larger than 500 mg. per month might produce the following symptoms and signs: Signs of oestrogen deficiency, including temporary amenorrhoea and senile vaginitis, and androgenic effects including hoarseness, hirsuties, acne, and enlargement of the clitoris. In almost all cases these phenomena regressed spontaneously after discontinuance of treatment. The authors suggested that the mechanism of testosterone action is threefold: inhibition of the gonadotrophic factors of the hypophysis resulting in failure of ovulation and suppression of the normal formation of oestrogen and progesterone, direct inactivation of the available oestrogens in the body, and the production of androgenic effects (virilism).

Effect on Cyclical Phenomena of the Female Genital Tract

J. W. Huffman and I. H. Bos confirmed the findings of others that testosterone propionate will inhibit functional uterine bleeding and menstruation in women when given in adequate dosage. Arrangement of the treatment can roughly control the duration and amount of the menstrual flow. It was also found that the rabbit ovary is stimulated by extract of pregnant mare serum, in spite of the previous administration of testosterone propionate. This observation, when correlated with the findings of Hamilton and Wolfe that testosterone decreases the gonadotrophic effect of the pituitary, adequately explains the mechanism of this androgen in inhibiting the cyclical phenomena of the female genital tract. Previous reports that testosterone inhibits functional uterine bleeding and menstruation were confirmed. Pregnant mare serum extract produced similar responses in the ovary of the rabbit before and after prolonged administration of testosterone. The action of testosterone propionate in inhibiting the cyclical changes in the female genital tract is probably not a direct one on the ovary, but rather a result of pituitary inhibition.

Excessive uterine bleeding—A. R. Abarbanel discussed the rationale for the use of testosterone propionate in the immediate treatment of excessive uterine bleeding. Testosterone propionate has already been proved to be more effective in the treatment of menorrhagia than any of the female hormones. Testosterone, like all the other sex hormones, is bisexual and in addition will act in the female either as an oestrogen or a progestogen. It controls haemorrhage from the uterus by its action on the myometrium. The myometrium surrounds the vessels, especially the proximal part of the spiral arterioles, and thus its contraction produces contraction of these vessels. It is the interruption of this process that produces excessive uterine bleeding, whatever the primary cause may be. Testosterone acts by contracting these myometrial elements and also by preventing rhythmic uterine contractions which pump the blood into the uterus. In 25 patients suffering from menorrhagia the bleeding was controlled by testosterone propionate in a dosage of 10 to 25 mg., given intramuscularly or divided between intramuscular and subcutaneous injections. After 2 to 4 days another deep subcutaneous injection was given. After 1 to 4 days the bleeding was usually controlled. At first a sharp increase in haemorrhage occurred in some cases. No testosterone should be given during the period or the condition will be aggravated. The drug may also be given by mouth in 10 mg. tablets. There were no signs of masculinization in this series, nor in a series of over 200 women similarly treated.

Abarbanel, A. R. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 243.

Binet, I., and Luxembourg, F. (1939) *Bull. Soc. méd. Hop. Paris*, **55**, 1016.

Fidelsberg, J., and Ornstein, L. A. (1940) *Endocrinology*, **26**, 46.

Geist, S. H., Salmon, U. J., Gaines, J. A., and Walter, R. I. (1940) *J. Amer. med. Ass.*, **114**, 1539.

Guirdham, A. (1940) *Brit. med. J.*, **1**, 10.

Hamilton, J. B., and Golden, W. R. C. (1939) *Endocrinology*, **25**, 737.

- Hooker, C. W., and Collins, V. J. (1940) *Endocrinology*, **26**, 269
 Howard, J. F., and Vest, S. A. (1939) *Amer. J. med. Sci.*, **198**, 823.
 Huffman, J. W., and Bos, I. H. (1940) *Endocrinology*, **26**, 259
 Korenchevsky, V., and Ross, M. A. (1940) *Brit. med. J.*, **1**, 645
 McCahey, J. F., and Rakoff, A. E. (1939) *J. Urol.*, **42**, 372
 Sharpey-Schafer, E. P. (1940) *Lancet*, **1**, 161
 Steinach, E., and Kun, H. (1940) *Lancet*, **1**, 688

Progesterone

Antitumorigenic Action

A. Lipschutz *et al.*, experimenting with castrated guinea-pigs, found that subcutaneous injections of oestradiol produce uterine and extrauterine fibrous tumours. If the animals were given oestradiol and progesterone the tumours were also produced, but to a lesser degree than in those receiving only oestradiol. They also stated that oestradiol produced fibromyomas less constantly and to a lesser degree in the non-castrated guinea-pig. Lipschutz *et al.* therefore concluded that progesterone exerts an antitumorigenic action and that uterine fibromyomas form in women as a result of the disturbance of the normal balance between the follicular and luteal hormones. They suggested that progesterone may prove useful in the treatment of fibromyomas.

Lipschutz, A., Murillo, R. and Vargas, I. Jr. (1939) *Lancet*, **2**, 420

SEXUAL BEHAVIOUR AND ABNORMALITIES

See also B I M P, Vol. XI, p. 110, and p. 60 of this volume

Perversions and Inhibitions

Male Homosexuality

Endocrine basis - S. J. Glass *et al.* investigated the sex hormone findings in 17 clinically diagnosed male homosexuals and in 31 normal males as controls. The sex hormone ratios were determined by quantitative assays of the urinary androgens and androgenic compounds in the urine. The homosexual group showed ratios which were distinctly lower than those of normal controls, the oestrogenic values were clearly higher among the homosexuals, whereas there were less striking differences in the androgenic values. In view of such highly suggestive hormonal differences the authors felt that such data pointed to a definite biological mechanism in homosexuality.

Glass, S. J., Denel, H. J., and Wright, C. A. (1940) *Endocrinology*, **26**, 590

SHOCK AND COLLAPSE

See also B I M P, Vol. XI, p. 126, Cumulative Supplement, Key No. 1400, Surveys and Abstracts 1939, p. 537, and p. 11 of this volume

Surgical Shock

Control of Water and Electrolyte Balance

J. R. Elkington *et al.* investigated the control of water and electrolyte balance in surgical patients. They determined the haematocrit value, the plasma protein, the plasma chlorides, and carbon dioxide combining power in the patient. From the last 2 figures the total base can be deduced, a fall in this figure indicates a serious extracellular base depletion. Rising haematocrit or plasma protein values indicates a serious depletion of extracellular water. The total volume should equal 20 per cent of the body weight. The type of intravenous fluid necessary can be deduced from these investigations. Elkington *et al.* investigated many patients with dehydration, intestinal obstruction, severe burns, and those about to undergo extensive gastro-intestinal operation. Appropriate treatment facilitated recovery and reduced the mortality rate in this series. Ten cases were reported in greater detail. The water and electrolyte balance is very difficult to control in patients with anaemia, hypoproteinaemia, and cardiovascular or renal disease. In cardiovascular disease, intravenous fluids must be given so as not to embarrass the heart, and those suffering from renal disease may not be able to tolerate large quantities of electrolytes.

Subendocardial Haemorrhages

H. I. Sheehan describes the subendocardial haemorrhages which occurred in about 75 per cent of the deaths from shock in the Glasgow Royal Maternity and Women's Hospital during the past 2½ years. There were in all 52 patients with shock from such causes as retained placenta and rupture of the uterus. The haemorrhages are localized to the left side of the interventricular septum, but sometimes occur on the musculi papillares and the trabeculae of the left ventricle. They were not present when the patient died rapidly. Old haemorrhages were also found in patients who had been shocked and subsequently died from some other cause. The haemorrhages were found in those who died of cerebral lesions such as thrombosis or embolism, and it is possible that they are produced by some nervous mechanism. The relation of the haemorrhages to the signs and symptoms of shock is not known.

Sheehan, H. I. (1940) *Lancet*, **1**, 831

Ilkington, J. R., Gilmour, M. T., and Wolff, W. A. (1939) *Ann. Surg.*, **110**, 1050

Treatment*Blood Studies as a Guide*

I. Scudder from much laboratory research and extensive clinical experience in the treatment of shock concludes that the one common denominator in the phenomena of shock, whether produced by damage of tissues, loss of fluid, haemorrhage, injection of toxins, destruction of the adrenal cortex, or stimulation of the sympathetic nervous system, is a rise in the plasma potassium. Experimental evidence, based on 28 cats, shows alterations in both concentration of the blood and of the blood potassium in shock; this inspissation of the blood usually precedes an increase in potassium. It would, however, be a mistake to ascribe shock to potassium poisoning alone, and it would probably be more correct to regard alterations in potassium in both the blood and the body fluids as a measure of profound cellular changes. In the treatment the rapid administration of large amounts of preserved blood stored too long would seem to be contra-indicated because of its high potassium content. In cases with a raised plasma potassium the use of eschatin, a highly purified extract of adrenal cortex and containing less than 1 part in 200,000 of adrenaline, and salt, given in repeated doses rather than a single large dose, proved beneficial, for prompt results. 20 c.cm. of eschatin were injected intravenously. All factors that tend to restore the altered physiological and physico-chemical states of the blood and to maintain a normal ratio between the extra-cellular sodium and intra-cellular potassium are beneficial in treatment, as they favour normal action currents.

Neo-synephrin

M. Kelly reported excellent results from the intravenous injection of neo-synephrin in collapse. The drug has an immediate effect on the pulse which becomes slow and full, and the patient at once feels better. This improvement can be maintained indefinitely by continuing the injection. Too rapid a rate of infusion, however, causes distress and an intolerable sensation in the head; the pulse becomes very slow and full. In an average case of moderate collapse 1.5 to 2.0 c.cm. of a 1 per cent neo-synephrin solution may be given each hour for as long as necessary. In urgent cases 1 litre of fluid containing 3 or 4 c.cm. of neo-synephrin solution may be given in 2 hours; if the need is less urgent 8 to 10 c.cm. may be given in 1 litre of fluid in 5 or 6 hours. The sole action of the drug appears to be on peripheral circulation, and no harmful effects occur even after prolonged administration.

Concentrated Serum

C. H. Best and D. Y. Solandt made an experimental investigation on the treatment of shock in dogs under deep nembutal anaesthesia; the shock was produced by histamine, by trauma with extensive haemorrhage, and by trauma with little or no haemorrhage, the existence of shock being determined by a blood-pressure below 50 mm. Hg. The treatment in severe shock was first the administration of a vaso-constrictor, pituitary extract temporarily to correct the vascular atony so that solutions introduced into the stream are not lost immediately into the tissue spaces; then concentrated dog's serum, which had been prepared by evaporating the

animal's serum to one-third of its normal volume, was given intravenously. This treatment was found to be successful, and it is believed that the results of these animal experiments should encourage a trial of pituitary extract and concentrated human blood serum on patients with severe traumatic shock.

Corticosterone

H. Selye and C. Dosne stated that experiments with rats indicated that pure corticosterone in aqueous solution was very effective in combating shock caused by surgical trauma and other means. Desoxycorticosterone, tested under similar conditions, was found to be ineffective. From these facts it appeared that the hydroxyl group on carbon atom 11 is important for the shock-combating of cortical steroids. The relative inefficiency of adrenal cortical extracts is probably due to the fact that the beneficial effects of the corticosterone, and possibly of other active steroids contained in them, are at least partly counterbalanced by harmful contaminating substances.

Paredrinol

P. Kunkel *et al.* found that the intramuscular injection of 25 mg. of paredrinol (α -N-dimethyl-*p*-hydroxyphenylethylamine) in 4 normal individuals prevented the collapse which occurs when sodium nitrite is administered, with the subject in the upright position. In 2 patients with severe postural hypertension, symptoms of cerebral anoxia were prevented by the use of paredrinol, and in 7 out of 10 cases of severe chemical shock resulting from infectious disease, the intramuscular or intravenous injection of from 15 to 50 mg. of the drug caused a rise in arterial pressure; only 2 of these cases, however, showed clinical improvement. In one case the drug was effective both in the collapse induced by an acute streptococcal pharyngitis and in the collapse subsequently induced by motionless standing. In cases of severe clinical collapse from 2 to 4 times the amount of the drug was required to cause a significant rise of blood-pressure, and even then the arterial pressure rarely rose to hypertensive levels. The authors concluded that paredrinol was a useful drug in the treatment of collapse due to pooling of blood within a dilated venous system. In shock due primarily to loss of fluid from the blood stream the drug may be not only ineffective, but even harmful.

Best, C. H., and Solandt, D. Y. (1940) *Brit. med. J.*, **1**, 799.

Kelly, M. (1939) *Med. J. Aust.*, **2**, 574.

Kunkel, P., Steidl, I. A., and Weiss, S. (1939) *J. clin. Invest.*, **18**, 679.

Scudder, J. (1940) *Shock, Blood Studies as a Guide to Therapy*, Philadelphia.

Selye, H., and Dosne, C. (1940) *Lancet*, **2**, 70.

SILICOSIS

See also B1 M P, Vol. XI, p. 133, and Surveys and Abstracts 1939, p. 537.

Aetiology

Silicosis Hazard in Dentistry

L. E. Siltzbach reported a case of silicosis occurring in a dental mechanic, aged 35 years. The patient had been employed for 19 years in polishing dentures, using for the purpose a grey powder known as 'pumice' which analysis showed to consist of complex silicates of various metals. There was no mechanism for removing dust in his work. His illness began with a productive morning cough followed by haemoptysis, loss of weight, and cyanosis. The sputum contained tubercle bacilli. The patient became weak and lost weight, and was admitted to hospital. On examination the chest was found to be increased in the antero-posterior diameter and there were impaired resonance, harsh breathing, and râles all over the chest. X-ray examination showed numerous soft, nodular densities throughout the lungs. There was a cavity containing fluid in the right lower lung. There was slight leucocytosis. The patient became worse and died 2 years and 4 months after the onset of the illness. Necropsy showed advanced silico-tuberculosis with hypertrophy

and dilatation of the right ventricle, chronic passive congestion of the viscera, and tuberculous ulceration of the small intestine

Siltzbach stressed the importance of controlling this new-found source of silicosis by providing an exhaust hood over the polishing apparatus and substituting the 'pumice' by some harmless powder

Siltzbach, L. E. (1939) *J. Amer. med. Ass.*, **113**, 1116

Clinical Picture

Influence of Silica on the Tubercle Bacillus

H. F. Heim de Balsac *et al.* discuss the question of the relation between the presence of silica and the growth and virulence of the *Mycobacterium tuberculosis*, and then report their experiments carried out *in vitro*. Since Schweinitz and Dorset in 1898 found an important quantity of silica in incinerated tubercle bacilli, some authorities have thought that silica favours the growth of the bacillus, whereas others, such as Polcard, stated that silicosis is only pulmonary tuberculosis that has become fibrous under the local influence of particles of silica. The various cultures undertaken by the authors (Heim de Balsac *et al.*) showed that a very slight, practically negligible, effect was exerted on the growth of *Mycobacterium tuberculosis* by enrichment of the media by silica, and inoculation of these bacilli into guinea-pigs did not have any influence on their virulence

de Balsac, H. F., Heim, Fernbach, I., and Rullier, G. (1940) *Bull. Acad. Med. Paris*, **123**, 365

SIMMONDS'S SYNDROME

See also B. E. M. P., Vol. XI, p. 145, and Surveys and Abstracts 1939, p. 538

Aetiology

Post-Partum Necrosis of the Anterior Pituitary

H. L. Sheehan stated that post-partum necrosis of the anterior pituitary is by far the commonest cause of Simmonds's syndrome. The necrosis usually follows a large haemorrhage and the signs and symptoms following depend upon the amount of tissue necrosed. If the patient again becomes pregnant the symptoms are cured because what is left of the anterior pituitary hypertrophies. These patients do not lactate, the external genitalia atrophy, and the uterus is superinvolved. Hypoglycaemia is sometimes present. Secondary sexual features and libido are lost and the patient becomes apathetic, dull, and sometimes prematurely senile. Other symptoms associated with the condition are low blood-pressure, anorexia, and hypochromic anaemia. Later mental changes may develop. Necropsy shows that the anterior pituitary has been converted into scar tissue and the thyroid, adrenals, and ovaries are atrophied.

Sheehan, H. L. (1939) *Quart. J. Med.*, **8**, 277

Morbid Anatomy

Associated with Dementia Praecox

M. M. Canavan reports a case of Simmonds's disease in a 72-year old man with dementia praecox. Marked emaciation occurred after a fracture of the femur. The Simmonds's syndrome lasted for 11 weeks. At necropsy the pituitary was small and oedematous. Microscopically the anterior lobe was found to consist chiefly of collapsed and dull polychromatic oedematous cells and there were many free nuclei and shadows of cell outlines. There was marked vacuolation of the cytoplasm of the acidophil cells, and a definite scarcity of basophils. The chromophobes appeared to be normal. The interstitial tissue showed no increase and the sinusoids were collapsed.

Canavan, M. M. (1940) *Arch. Path.*, **29**, 310

Clinical Picture

Atrophy of Pituitary following Tuberculosis

Atrophy, following tuberculosis, of the pituitary, secondary to primary infection of the lungs, was recorded by W. Berblinger, in a woman, aged 52, with Simmonds's syndrome. The right lung showed obsolete tuberculosis; there was emaciation with atrophy of the pituitary and adrenals and almost complete absence of pubic and axillary hair. Histologically the pituitary showed typical tuberculosis with the presence of acid-fast bacilli. It is suggested that the recognition of tuberculosis of the pituitary is of practical importance, for the curative capacity of the infection in the lung and also in the pituitary might, if suitable hormone treatment had been employed, have prevented the fatal issue. The author prefers the name Simmonds's syndrome to pituitary cachexia, because emaciation is not present in all cases.

Berblinger, W. (1939) *Schweizer med. Wchnschr.*, **20**, 1217.

— (1940) *Brit. med. J.*, **1**, 697.

SKIN DISEASES. AFFLICTIONS DUE TO INSECTS AND ACARINES

See also B. I. M. P., Vol. XI, p. 149.

Delousing

Temperatures Lethal to Lice

P. A. Buxton found that the lowest temperature fatal to all lice was 51.5 °C for 5 minutes, 49.5 °C for 10 to 30 minutes, and 46 °C for 45 minutes to one hour. Female lice exposed to temperatures just below death point laid infertile eggs. For eggs under 5 days old the lowest fatal temperatures for eggs were 53.5 °C for 5 minutes, 52 °C for 10 minutes, and 50 °C for 30 minutes. With older eggs, incubated 8 or more days, the lethal temperatures were lower. Ordinary laundry processes, as applied to cotton goods, should generally be sufficient to kill all stages of the insect. The temperatures at which woollens are washed, however, is such that they would probably be ineffective. Dry cleaning is doubly safe, since both the solvent employed (carbon tetrachloride, petrol, etc.), and the subsequent treatment in hot drums, would be lethal to lice and eggs.

Buxton, P. A. (1940) *Brit. med. J.*, **1**, 341.

Scabies

Treatment

Rotenone.—C. C. Thomas and F. E. Miller claimed that rotenone, a constituent of derris root, is an effective, non-odorous, and non-irritating agent for treating scabies. The substance, which has been widely used for various veterinary conditions, is colourless, crystalline and non-nitrogenous, and is stated to have the empirical formula, $C_{21}H_{22}O_6$. In the form of 1 or 2 per cent lotions, it produced prompt cure in 24 unselected cases of scabies, some of which presented most severe secondary pustular and dermatitic complications. After bathing, the lotion was applied night and morning for 4 applications.

Creolin.—I. Jane recommended the use of creolin in the treatment of scabies, on account of its cheapness, simplicity, efficacy, cleanliness, and the minimum of inconvenience for the patient and economy in time. A 20, 25, or 33 per cent emulsion of creolin in distilled water is employed for children, women, and men respectively. Before re-treating the patient applies the preparation lightly, without friction, to the whole of the body, except the face, and allows it to remain during the night. Treatment is repeated on 3 consecutive nights, and the bed clothes are not changed until the end of treatment. The author claims that cure is constant and dependable.

Jané, F. (1940) *Urol. cutan. Rev.*, **44**, 181.

Thomas, C. C., and Miller, F. E. (1940) *Amer. J. med. Sci.*, **199**, 670.

SKIN DISEASES : LOCALLY INOCULATED INFECTIONS

See also B.E.M.P., Vol. XI, p. 183, and Cumulative Supplement, Key Nos. 1409-1410.

Streptococcal Dermatitis

J. M. Flood and J. H. Stokes report on 6 cases of severe dermatitis, cultures from which showed haemolytic streptococci, and which were treated with sulphanilamide. The 6 cases were described as follows: (i) a patchy papulo-vesicular dermatitis on the dorsum of hands, wrists, and arms, present for one month, becoming worse under local treatment, the patient was admitted to hospital with extension of the process to shoulders, back, chest, face, and left ear, (ii) a recurrent dysidrotic eruption on the hands and feet with secondary infection (8 years) with latterly frequent pustular exacerbations, (iii) an extensive pustular sycosis (4 months) which under local treatment became worse with bullous involvement of neck, chest, and back; (iv) a severe phenol burn of the hands followed (one month) by a deep pustular and bullous eruption of hands and feet, (v) a generalized erythroscumous dermatitis with weeping and crusting about the scalp, ears, face, and back (3 months), (vi) a patchy, weeping eruption of an amputation stump (6 years) with an attack of seborrhoeic dermatitis of the scalp, face, back, and chest. Cultures from all these cases showed haemolytic streptococci.

Treatment

Sulphanilamide—Under sulphanilamide therapy marked improvement was shown, the authors emphasize that this drug does not cure the patients, but only brings the condition under control, when therapy is directed towards the other varied contributing factors. With such a small series of cases it is not possible to determine what dosage of sulphanilamide is necessary for a good therapeutic result. The authors suggest the following dosage: 1st day 7 g., 2nd day 6 g., 3rd day 5.3 g., 4th to 7th day 4 g., thereafter 3 g. per day. It is well to continue the drug for one week after apparent cure. Three cases reacted to large dosage with severe toxic symptoms and the authors believe it is essential to have the patient in hospital, where a careful watch can be kept on the temperature and blood-count.

Flood, J. M., and Stokes, J. H. (1939) *Brit. J. Derm.*, **51**, 359.

Granuloma Pyogenicum*Treatment*

X-rays—D. Eisen reports 4 cases of granuloma pyogenicum, treated successfully by X-rays, and summarizes the present state of knowledge about this infection, first described as botryomycosis hominis by Poncet and Dor in 1897. The 4 patients (3 housewives, and 1 man, the latter with a definite history of injury) had an average age of 36 years, and were treated in 1936 and had not relapsed since. The total dosage varied between 444 and 750 r., divided into 4 or 5 treatments at weekly intervals, either 80 kv. without filtration or 100 kv. with 1 mm. aluminium filtration used with 5 ma. at 30 cm. distance. The lesions disappeared about a week after the 4th or 5th treatment. About 400 cases have been recorded, but it is probably more frequent, women are twice as often affected as men, and in half the cases there is a history of trivial injury, such as a prick with a needle. The infective agent is not finally settled, but staphylococci have been often suggested. The exposed parts of the body—face and hands—are usually attacked. There is one small red nodule which may be pedunculated. Histologically the lesion is granulomatous with numerous blood channels, so that haemorrhages may occur. Treatment has usually been on the lines of curettage, cauterization, electro-desiccation, or carbon dioxide snow. X-ray treatment, which is painless and not operative, when mentioned at all, has been usually dismissed very briefly.

Eisen, D. (1940) *Canad. med. Ass. J.*, **42**, 528.

Poncet, A., and Dor, L. (1897) *Rev. Chn., Paris*, **18**, 996.

SKIN DISEASES: TUMOURS

See also B.E.M.P., Vol. XI, p. 200, Cumulative Supplement, Key Nos. 1412-1415, and Surveys and Abstracts 1939, p. 539

Innocent*Warts*

Urea therapy—F. M. McKay found that a sterile 50 per cent solution of urea was useful in removing warts. From 0.1 to 0.3 c.c. was injected intracutaneously at the base of the wart. In a group of 6 patients with 19 warts the growths were effectively and permanently removed, leaving practically no scar. Disappearance of the warts occurred in from 5 to 15 days. This method was employed because of the virucidal effect of strong solutions of urea, but it is uncertain that this virucidal effect is the mechanism involved in the removal of warts with urea.

Derived from Nerve Tissue

Glomangioma—A. C. Lendrum and W. A. Mackey reported 15 cases of glomangioma. The onset of the tumour is often related to trauma and usually occurs on a limb. It is painful and, if situated under the skin, may be seen as a bluish nodule which often engorges during a painful attack. Other vasomotor phenomena may be present such as the affected part being colder than the rest. The pain starts as a tingling sensation, but gradually becomes more and more severe and then begins to radiate, not along any nerve pathway, but diffusely through the affected part. Microscopically the tumour is composed of blood spaces characterized by the presence of large cuboidal (glomus) cells in the walls. It is benign and may be efficiently treated by complete excision.

Lendrum, A. C., and Mackey, W. A. (1939) *Brit. med. J.*, **2**, 676.

McKay, F. M. (1940) *Arch. Derm. Syph., N. Y.*, **41**, 736.

Innocent Infective Conditions*Boeck's Sarcoidosis*

F. F. Cotter reviews Boeck's sarcoid and reports a case in a negro male, aged 18 years, in whom visceral lesions were found at necropsy. His illness began with fatigue and dyspnoea on exertion followed by oedema of the ankles, orthopnoea, loss of weight, and cough with mucoid sputum. Examination showed enlargement of the heart and liver, and moderate enlargement of the lymph nodes, and dullness and râles in the lungs. There was anaemia, a positive Wassermann reaction, and a negative tuberculin reaction. The patient became worse, auricular fibrillation supervened and finally death from heart failure. Necropsy showed Boeck's sarcoid with nodules in the myocardium, lungs, liver, spleen, testes, lymph nodes, and beneath the skin of the right forearm. The lesions were composed of multiple discrete tubercles and many confluent groups of tubercles. The aetiological factor in this case was unknown, but the myocardial lesions were similar to those reported in two cases of uveo-parotitis.

G. T. Harrell studied 11 cases of generalized sarcoidosis of Boeck over a period of 4 years. The cases included 2 patients who had been well clinically for 2 years. He found definite changes in calcium, protein, and phosphatase content of the blood, but the phosphorus and non-protein nitrogen were not altered. In cases in which the condition was active the cholesterol content was generally low, or normal. Bilirubin-tolerance tests showed retention, whereas calcium-tolerance tests gave varied results. In some cases substances resembling Bence Jones protein were present in the urine. Investigation of the blood confirmed low or normal white blood-cell counts, neutropenia, eosinophilia, monocytosis, and increased sedimentation rate.

Epidermolysis Bullosa

R. R. Kierland and M. W. Harrison reported a case of epidermolysis bullosa with elevated urinary porphyrins. It is a rare disease, and only 5 cases have been reported in the recent literature. Any part of the skin or mucous membranes may be affected,

and some part is played in the condition by consanguinity of the parents. The case reported occurred in a 21-year-old man of Jewish descent. He had had recurrent bullous lesions of the feet since the age of 1 year. Occasionally they had occurred on the heels or near the ankles. The contents of the bullae were usually serous, though sometimes sanguineous. There was no family history of the disease, but the parents were cousins. No septic foci could be found and there were no dystrophic changes elsewhere on the skin. The only abnormal laboratory investigation found was the elevation in urinary porphyrins.

Cotter, I. F. (1939) *Arch. intern. Med.*, **64**, 286

Harrell, G. T. (1940) *Arch. intern. Med.*, **65**, 1003

Kierland, R. R., and Harrison, M. W. (1940) *Proc. Mayo Clin.*, **15**, 313

Carcinoma

Prognosis

S. Warren *et al.* report 829 treated cases of cutaneous carcinoma, not verified by biopsy. 84 per cent were followed for 5 years, and there were 57 per cent of 3-year and 48 per cent 5-year cures of all tumours treated. If the cases lost and dead of intercurrent disease are counted as cures, the 5-year cures would be 84 per cent, if they are entirely excluded, the percentage would be 76. Recurrences occurred in 13 per cent of cases showing primary healing, followed up for one year or more. Primary healing occurred in 94 per cent of the lesions followed for one year or more. More than 25 per cent of the deaths from cutaneous carcinoma occurred after primary healing. Primary healing should not be considered as a criterion of cure. Failures are largely due to the use of very light filtered radon applied to the surface in inadequate dosage. X-rays, or radium employed at a distance, would have given greater depth doses, and probably therefore better results.

Warren, S., Simmons, C. C., and Rea, S. L. (1940) *J. Amer. med. Ass.*, **114**, 1619

Malignant

Melanotic Carcinoma

Incidence in coloured races. Hamilton Baxter reviews the subject of malignant melanoma in the coloured races, which has been regarded as specially rare, numerous statistics are brought forward to show that it is commoner than has been thought. Most malignant melanomas arise from a naevus (benign melanoma) which, as Masson has shown, originates by proliferation of the entire end-apparatus of the sensory nerves of the skin, especially the cells of Meissner's corpuscles in the dermis. The naevus cell is neuro-ectodermal and may be pigmented (melanoblasts) and not related to the nerve endings (naevus cells) and not pigmented. The degree of pigmentation of the tumours depends on which of these two cells predominates and does not bear any relation to malignancy. Out of 224 collected cases it was possible to decide the point of origin in 170, in 111, or 65 per cent, of these the growth arose in the foot, especially on the sole, in 16 in the lower extremity (exclusive of the foot), in 16 in the eye, in 13 in the upper limb, and in 8 in the head and face. The preponderating incidence in the foot has been ascribed to injury, it has also been suggested that in the coloured races malignant melanomas are prone to arise in areas where there is a transition from a darker to a lighter colour. A case of a malignant melanoma primary in the mouth—extremely rare in a negro—with a metastasis the size of a golf ball in the lower lobe of the right lung, was reported.

According to G. T. Pack and F. E. Adair melanoma is comparatively rare in the negro race except for some reports from Africa; they collected 34 cases, excluding African cases, and found that there was a tendency for these tumours to occur in parts of the body that contain least pigment, such as the soles of the feet and the matrices of the nails.

Primary Cutaneous Xanthoma and the Melanomas

N. C. Foot discusses the confusion about the nature of the large group of tumours and tumour-like structures known as xanthomas, and the question whether or not all these tumours have the same histological nature. They have been regarded as

granulomas and a manifestation of hypercholesterolaemia (Gruenfeld and Seelig) and Haagensen divided them into primary xanthomas of 5 subgroups and secondary xanthomatoid deposits of lipin-containing histiocytes in connexion with inflammatory or degenerative processes. Foot's observations lead to the conclusion that the cutaneous xanthomas are distinct from the others, he found by a special modification of Ramón y Cajal's silver method of block impregnation that these tumours contain non-medullated nerve fibres. The suggestion is made that these tumours are in a phylogenetic position intermediate between that of the melanoma, which is terminal on the nerves, and the lemmoma and neurofibroma which may occur along their course. In one tumour a well-developed melanoma covered a xanthoma, and microscopically these xanthomas contain pigmented melanophores in the connective-tissue septa of the xanthomas and sometimes in the rete spaces with the foam cells.

Cutaneous Carcinomatous Metastases Confined to Scalp

H. Montgomery and R. R. Kierland report 4 cases, 2 in women (both aged 58) and 2 in men (aged 58 and 71) with carcinomatous metastases in the scalp but in no other part of the skin of the body, in each of these 4 cases there were more than one secondary tumour in the scalp, the primary growth being abdominal in 3 and in the left lung in the fourth. It is pointed out that statistics as to the incidence of cutaneous metastases vary from 1 to 3 per cent, and that such metastases usually occur in the neighbourhood of the primary carcinoma. Some primary carcinomas, however, especially mammary carcinoma, show a predilection for the scalp. The metastases in the scalp must be diagnosed from cylindroma which is characteristically multiple but rarely becomes malignant, from sebaceous cysts of the scalp which give rise to a squamous-celled carcinoma in from 2 to 9 per cent, and from primary carcinomas of the dermal appendages (sweat and sebaceous glands).

Baxter, H. (1939) *Canad. med. Ass. J.* **41**, 350.

Foot, N. C. (1939) *Amer. J. Cancer*, **37**, 425.

Gruenfeld, G., and Seelig, M. G. (1934) *Arch. Path.* **17**, 546.

Haagensen, C. D. (1932) *Amer. J. Cancer*, **16**, 1077.

Montgomery, H., and Kierland, R. R. (1939) *Proc. Mayo Clin.* **14**, 431.

Pack, G. T., and Adair, I. F. (1939) *Tumours of the Hands and Feet*, London, p. 56.

SPEECH DEFECTS

See also B. F. M. P., Vol. XI, p. 294, and Surveys and Abstracts 1939, p. 542.

Relation to Hearing Defects

I. W. Voorhees states that, although speech and hearing defects are often inter-related, errors of speech are twice as common, or even more so, as defects in hearing. Anatomical defects such as a cleft palate may lead to faulty speech. Much deafness in childhood is due to infection of the tonsils and adenoids, and otitis media and mastoiditis are common complications causing deafness. Sinusitis and swelling of the nasal mucosa may lead a child to 'talk through his nose' and so produce vocal defects. Speech defects may be associated with loss of hearing for certain frequencies, either high or low pitch, successful treatment of these cases largely depends on proper teaching. Severe deafness in childhood may be congenital or acquired; much can be done for these children, but teaching is often difficult because they shrink from contact with normal persons. Profound deafness in adult life is prone to induce voice changes. Voorhees comments upon the lack of well-modulated voices among ordinary individuals and hopes that in time more people will be encouraged, and expected, to speak pleasantly.

Voorhees, I. W. (1940) *Arch. Otolaryng.*, Chicago, **31**, 7.

Treatment*Hypnosis*

J. J. Levburg reviews the use of hypnosis in the treatment of speech disorders. In about 75 cases, mostly of stammering and stuttering, the results were very good: hypnosis shortened the ordinary period of speech training and some patients responded after as few as 2 sessions. Mental and physical hygienic measures were combined with suggestion under hypnosis, 6 cases in which the treatment was successful being reported in full. Stress was laid on the importance of a sound knowledge of psychiatry and otolaryngology and the possession of a musical ear by the practitioner undertaking these cases.

Levburg, J. J. (1939) *Arch. Otolaryng.*, Chicago, **30**, 206.

SPINAL CORD DISEASES

See also B E M P., Vol. XI, p. 302, and Surveys and Abstracts 1939, pp. 120 and 543

Tumours*Primary Melanoma of the Spinal Cord*

D. G. DaCosta and J. G. Love of the Mayo Clinic record with a commentary a case of an intramedullary melanoma of the spinal cord, which may be regarded as primary, at least from a clinical point of view. A middle-aged woman in 1917 had a motor car accident which injured her back, necessitated rest in bed for 6 months, and left behind numbness of the toes of the right foot; this disappeared, but the other foot became similarly affected. In 1936 both feet were numb, and the sensory changes spread. On admission to the Clinic in June, 1938, the clinical picture showed complete spastic paraplegia, urinary and faecal incontinence, and absence of sensation to touch, pain, and temperature from the toes to the fifth thoracic segment, above which there was an area of hypaesthesia up to the third thoracic segment. At laminectomy, centred over the fifth thoracic vertebra, the cord was seen to be bluish opposite the sixth dorsal vertebra and a tumour was partially removed; it contained black material which was later reported to be a typical melano-epithelioma with chiefly spindle-shaped cells, irregularly arranged in whorls and some with giant nucleoli. During the operation when the character of the tumour was seen, the possibility that a tumour in the dorso-lumbar region might have a bearing on the case led to its removal, but it was a non-pigmented fibroma. The patient ran an uneventful post-operative course. The primary or secondary character of the melanomas of the central nervous system was discussed in the light of authoritative opinions. Formerly they were all regarded as secondary, and when no obviously primary melanoma was detected, a small apparently quiescent cutaneous mole or choroidal melanoma was suspected. But chromatophores or melanoblasts of the normal pia mater and the adventitia of the pial vessels were a possible origin for melanomas. Reference is made to P. Masson's view that even cutaneous melanomas are of nervous origin, from the tactile corpuscles of the skin.

DaCosta, D. G., and Love, J. G. (1939) *Proc. Mayo Clin.*, **14**, 628

Masson, P. (1926) *Ann. d'anat. path.*, **3**, 417

SPINE, DISEASES AND DEFORMITIES

See also B E M P., Vol. XI, p. 361, and Surveys and Abstracts 1939, p. 544

Tuberculosis (Pott's Disease)*Morbid Anatomy*

Multiple pathological fractures—R. I. Harris and H. S. Coulthard report a case of tuberculous disease of the spine in a man, aged 54, with unusual features. Radiologically the spinal lesion suggested malignant disease, painless fractures of the ribs occurred, and the pus from their neighbourhood contained tubercle bacilli. The necropsy showed tuberculous necrosis of the body of the ninth dorsal vertebra.

18 fractures of 9 ribs on the left side and 5 on the right side without any predominant site in the ribs. There were not any fractures in the rest of the skeleton. The lungs were free from tuberculosis, but the visceral pleura over the apex of the lower lobe of the left lung had been invaded by direct extension from the spinal abscess. There was a terminal miliary infection involving the liver and spleen throughout their substance and in the right adrenal there was a small tuberculous nodule, otherwise the rest of the body was free from miliary tuberculosis. The portal of entry for the tubercle bacilli which reached the spine was not evident.

Harris, R. I. and Coulthard, H. S. (1939) *Canad. med. Ass. J.* **41**, 434

Prolapse and Calcification of Intervertebral Disks

Protrusion of Disk

B. Stookey pointed out that the so-called ventral extradural cervical chondroma, first recognized as a clinical entity in 1928, is now believed to be, not a neoplasm, but a portion of the nucleus pulposus protruding through the annulus fibrosus into the vertebral canal. These protrusions press on the spinal cord and nerve roots, or both, and give rise to 3 distinct syndromes, (a) bilateral ventral pressure, (b) unilateral ventral pressure; and (c) pressure on nerve roots. Most cases of cervical disk herniations occur in men of late middle age, the youngest of the author's patients was 44, and the oldest 68. Diagnosis is often difficult, because the signs and symptoms may closely resemble those of intrinsic disease of the cord. Removal of the herniated portions is best effected through a Taylor's hemi-laminectomy.

H. B. Macey investigated 100 cases in which posterior protrusion of an intervertebral disk was apparently responsible for symptoms. The pathological picture of a posteriorly protruded disk is that of nerve compression. The most prominent finding in this series was degeneration of the fibrocartilage. The pathological appearance at operation is that of a firm hard protrusion at the postero-lateral intervertebral space. On exposure by incision of the posterior longitudinal ligament, this protrusion may be seen to extrude into the wound, or it may be so firmly adherent as to require excision for its removal. The clinical picture includes a 'low backache', the initial onset of which is attributed to an injury sufficiently severe to be remembered. In some cases the chief symptom is sciatica, in others there may be both backache and sciatica, with or without a history of injury. The sciatic pain is aggravated by activity, coughing, sneezing and defaecation, which induce traction on the nerve roots. Most patients become free from pain on lying absolutely motionless. Of 98 cases in which radiographic examination with radio-opaque oil was carried out, a positive defect was found in 93. The most important finding in neurological examination was a diminished tendo Achillis reflex. The author considered the following test to be significant: sudden unexpected hypertension at the lower lumbar vertebrae may cause pain over the course of the affected sciatic nerve. Treatment consists of laminectomy and removal of the ligamentum flavum and the disks, the articular facets being preserved.

J. G. Love and M. N. Walsh, in an analysis of 500 consecutive cases of intraspinal protrusion of intervertebral disks operated on, found that 58 per cent of the patients gave a history of injury of the back. The three neurological signs most helpful in the diagnosis of protrusion of a lumbar disk are Lasègue's sign, which was positive in 84 per cent of cases, sciatic tenderness which was present in 64 per cent of cases, and diminution or absence of the tendo Achillis reflex on the side of the pain, the last being noted in 60 per cent of cases. In only 25 per cent was there any muscular weakness, and sensory loss was detected in only 21 per cent. Negative neurological results were obtained in 20 per cent, except for a positive Lasègue's sign or sciatic tenderness, or both.

X-ray Diagnosis

W. E. Chamberlain and B. R. Young describe the technique of the test for the diagnosis of protrusion of an intervertebral disk, by intraspinal injection of air. Whenever operation was performed on the 300 cases so diagnosed the diagnosis and the level of the lesion were found to be correct. The procedure is harmless as no irritating substance is introduced into the spinal canal. Air, and even more readily oxygen, are easily absorbed from the subarachnoid space. The spinal fluid is replaced

by air, 40 to 50 c.cm. being usually needed to fill the lumbo-caudal sac in the adult. 'Overexposed' films are best used to give radiographs showing good contrast and detail.

Relative merits of oxygen and lipiodol—S. N. Berens argues that oxygen is better than lipiodol for visualization of deformities of the dural sac, such as protrusion of intervertebral disks and hypertrophy of the ligamentum flavum. The following points are given for and against the use of lipiodol and oxygen. Lipiodol gives a clearer picture, is more accurate for small lesions, is easy to use, is not painful, and is useful in any part of the spinal canal. On the other hand operation is necessary for removal of lipiodol, and inflammatory reaction results if oil is not removed, and if all the oil is not removed subsequent radiographs show its presence. The advantages of oxygen are that it reveals all medium-sized or large deformities of the dural sac, such as would unquestionably require surgical treatment, there are no after-effects, and it may be employed several times if necessary. On the other hand, it requires a powerful X-ray apparatus, it is not always as clear as lipiodol, it is painful and requires a sedative, it is most useful in lumbar, sacral, and lower dorsal deformities, and it requires more time and trouble to perform. In a few cases the use of lipiodol may be necessary for localization, or for border-line cases.

Clinical Picture

R. G. Spurling and F. K. Bradford describe the clinical results of herniation of the nucleus pulposus at the level of the 4th and 5th lumbar interspaces. The most outstanding symptom is severe sciatic pain which may be aggravated by coughing and straining. The onset is associated with trauma or sudden change in position of the trunk. Movement accentuates the pain. Paraesthesiae are very important as localizing signs. In herniation at the 4th or 5th lumbar interspace tingling, prickling, cold, or numb sensations occur below the knee in the lateral aspect of the leg or foot. Weakness is not common and may be due to disability from the pain. The lumbar spine is stiff, but this may also occur in other articular disease in this region. Of more importance diagnostically are persistence of the knee in flexion (Lasegue's sign), the paraesthesia, and diminution or absence of the ankle jerk. Sometimes pressure on the spines of the 4th and 5th lumbar vertebrae produces sciatic pain. Hyperaesthesia of the antero-lateral aspect of the leg including the great toe may occur. If the 1st and 2nd sacral nerves are involved the postero-lateral aspect of the leg and the lateral part of the foot are included. These signs may also be produced by neoplasm along the course of the sciatic nerve, pelvic and rectal disease, and bony disease of the part. Herniation of the nucleus pulposus must be differentiated from these conditions.

Berens, S. N. (1940) *Northw. Med., Seattle*, **39**, 160.

Chamberlain, W. L., and Young, B. R. (1939) *J. Amer. med. Ass.*, **113**, 2022.

Love, J. G., and Walsh, M. N. (1940) *Arch. Surg., Chicago*, **40**, 454.

Macey, H. B. (1940) *Arch. Surg., Chicago*, **40**, 433.

Spurling, R. G., and Bradford, F. K. (1939) *J. Amer. med. Ass.*, **113**, 2019.

Stookey, B. (1940) *Arch. Surg., Chicago*, **40**, 417.

Retropulsion of Nucleus Pulposus

S. Pappworth reviews critically reports on retropulsion of the nucleus pulposus and the advisability of performing a laminectomy for this condition. Although the lesion undoubtedly exists, it is not conclusively proved that it gives rise to symptoms. According to various writers, it occurs at any time during adult life, but at this time of life the lesion cannot be of great significance because a 'normal' disk in the 'normal' spine of a 'normal' adult is very rare. The symptoms ascribed to it vary widely—muscular weakness, paralysis, and loss of the ankle-jerk. The protein-content of the cerebrospinal fluid has been raised in some cases. The differential diagnosis has been complicated by observers who attribute symptoms to the retropulsion when in fact it was only incidental, for example, such conditions as subacute combined degeneration of the cord which are really responsible for the symptoms. On the question of laminectomy quoted cases show that it may not

do any good, and patients may die from wound infection. More conservative measures are therefore indicated.

Pappworth, S. (1939) *Brit. med. J.*, **2**, 1038.

Scoliosis

Aetiology

Pyogenic non-tuberculous empyema - S. Selig and I. Arnhem report 5 cases of scoliosis after pyogenic non-tuberculous empyema in a series of 65 patients with the latter condition. Scoliosis developed only in those in whom the empyema was chronic and required multiple operations so that the shape of the thorax was altered; in all the patients affected the empyema had occurred under 12 years of age.

Three of the cases were of the type occurring after an empyema, that is, with the concavity on the side of the empyema, two being extreme. The other 2 cases followed thoracoplasties, and there the curves were again typical with the convexity towards the side of the rib resections. The curvature was persistent and in the severe cases progressed in spite of treatment with special jackets.

Prevention

R. Ledent reviews the cases of scoliosis which were due partly, if not entirely, to conditions in school life. Schools are often described as factories in which scoliosis is acquired; this is an exaggeration, but nevertheless predisposed children, when subjected to ordinary school life, develop scoliosis. The author concludes that all schools should have specialist teachers in attendance who are able to detect any early malformation and to aid in its prevention by modern gymnastic methods.

Treatment

Bone traction - F. Goodwin and D. K. Barnes described a new method of treating scoliosis by bone traction. A complete X-ray investigation of the spinal curvature is made to determine how high and low the ultimate fusion may be made. A plaster cast with anterior and posterior hinges is then applied. The cast is then wedged until the maximal amount of correction has been obtained. This correction is then fixed by applying additional plaster. On the side of the convexity there is now incorporated in the plaster a special apparatus called a "pusher". A window is cut over the vertebrae which are to be fused, and a Hibbs' fusion is carried out. Additional bone for grafts has generally to be removed from the tibia. The spinous processes of the three vertebrae forming the apex of the curve are carefully preserved. A groove is made around the bases of these spinous processes, and over them pliable stainless-steel 20 gauge wire is looped. An aneurysm needle is then passed through the skin and muscles on the side of the back in the posterior axillary line. The wire is threaded in the needle and pulled back through the muscle and skin and through a hole in the cast. The three wire loops are then attached to an apparatus that will allow traction to be placed on them, and the wires are tightened daily until complete correction has been obtained. As a rule the maximal possible correction is obtained. The wires remain in place until firm bony ankylosis occurs. The plaster cast is retained for 3 months after the last operation, and the patient is then supported by corsets for another 12 months. This method is suitable for children of 12 years and over. It was employed in 6 cases and, in each, greater correction was obtained than is often possible with the standard technique, and in no case was rotation increased.

Goodwin, F., and Barnes, D. K. (1939) *St. Louis Med.*, **23**, 1939.

Ledent, R. (1939) *Bru. méd.*, **19**, 1185.

Selig, S., and Arnhem, I. (1939) *Arch. Surg., Chicago*, **39**, 798.

Vertebra Plana

R. Fawcett reports with many fine radiograms a case of a child, aged 4 years, with Calvé's osteochondritis vertebralis (vertebra plana) associated with cystic changes in the femora, the left humerus, right ilium and the parietal and occipital regions of the skull. The first lesion of the spine to appear was in the 3rd lumbar vertebra, later in the 4th lumbar and the 2nd and 3rd cervical vertebrae. There was spina bifida occulta of the sacrum. Both kidneys contained calculi, the blood calcium

was slightly raised. The child fell on her outstretched left arm and complained of pain in the shoulder; radiological examination showed a fracture without displacement just below the surgical neck of the humerus through an area of cystic change; this fracture united satisfactorily with the texture of the bone almost normal. There was not any evidence of tuberculosis or syphilis.

Fawcett, R. (1940) *Brit J Radiol*, N S, **13**, 172.

Spondylolisthesis

Aetiology

M. Batts discussed the aetiology of spondylolisthesis. He stated that it is usually supposed to be due to a congenital defect, namely non-fusion of the centres of ossification of the 4th or 5th lumbar vertebrae. In many cases of spondylolisthesis a separate neural arch in the affected vertebra has been found. The author examined 200 foetal spines and in no instance found a double ossification centre for the half of a neural arch in the 4th or 5th lumbar vertebra which has been held to be the cause of its separation. In one case only was there an accessory centre of ossification in the neural arch, on one side only in a 3rd lumbar vertebra. The author proposed that spondylolisthesis is due to an inherent weakness of the isthmus of the neural arch which is developed before birth but concluded that the aetiology of the condition is probably not based on a congenital defect.

Batts, M. (1939) *J. Bone Jt Surg*, **21**, 879.

Hypertrophy of Ligamentum Flavum

M. B. Dockerty and J. G. Love report on 50 cases of hypertrophy of the ligamentum flavum, 25 normal lumbar ligamenta flava obtained at necropsy being employed as controls. In the first group the ligaments were found to be thickened, 70 per cent of them being thicker than the thickest ligament in the control series. Histological examination showed longitudinal splitting and fraying of the elastic fibres. At the same time the fibres had taken on the appearance of connective tissue, in some cases nearly all the elastic tissue being replaced by it. The authors referred to this change as 'fibrous'. Another change often seen was hyaline thickening in the walls of the blood vessels. Fatty infiltration around the vessels near the attachment of the ligament was seen in 12 cases. Calcification occurred in 3 and cartilage formation in 2 instances. It is suggested that the inaccurate term 'hypertrophy' should be superseded by 'thickening and fibrosis'.

Dockerty, M. B., and Love, J. G. (1940) *Proc Mayo Clin*, **15**, 161.

Osteomalacia Columnae

Aetiology and Clinical Picture

I. Meulengracht reports on a series of cases of osteomalacia. The osteomalacial changes were mainly in the vertebral column. Symptoms were backache, and pain in the thigh which sometimes occurred in acute attacks with spontaneous fractures. He observed a concavity in the back, sometimes in connexion with a kyphosis or lordosis, and the patients complained of loss of stature. X-ray examination showed lack of calcium in the skeleton, especially in the vertebrae, which appeared to be smaller than normal and to have biconcave excavations or irregular deformities. Some cases showed an osteoarthritis of the spinous process in the lumbar region, caused by the shortening and concavity of the lumbar spine. In some cases the disease is due to a dietetic deficiency in calcium and vitamin D; in the other instances disorder of the digestive tract, such as achylia gastrica or change in the absorption from the intestine, is mainly or partly responsible for the symptoms. Meulengracht calls this type of osteomalacia either 'osteomalacia achylia' or 'osteomalacia e abuse laxantium'. Treatment with calcium or vitamin D was effective.

Meulengracht, E. (1939) *Wien. klin. Wschr.*, **52**, 725.

SPLFEN DISEASES

See also B.E.M.P., Vol. XI, p. 401, and Surveys and Abstracts 1939, p. 546

'Agnogenic' Myeloid Metaplasia

H. Jackson *et al.* described 10 cases of what they term 'agnogenic' myeloid metaplasia of the spleen, a condition characterized by a slowly progressive enlargement of the spleen with a blood picture which simulates that of myelogenous leukaemia, or, more rarely, of acquired haemolytic jaundice. The average duration from onset till death was 10.8 years. In 4 cases the symptoms had been present for 15 years. The chief symptoms were weakness, abdominal distress, and a haemorrhagic tendency. The chief signs were a progressive enlargement of the spleen, a moderately elevated or slightly depressed white-cell count, and the constant presence of immature red and white cells in the blood stream. Pathologically the spleen showed marked myeloid metaplasia, namely scattered foci of immature red and white cells and megakaryocytes throughout a slightly or markedly fibrosed organ. The bone marrow was fibrotic, hyperplastic, aplastic, or normal, and in no case was it suggestive of leukaemia. Neither splenectomy nor X-ray therapy was effective.

Jackson, H., Parker, I., and Lemon, H. M. (1940) *New Engl. J. Med.*, **222**, 985

Septic Infarct

R. dos Santos describes a case of septic infarct of the spleen. The diagnosis was made on sudden pain in the left hypochondrium, fever, enlargement of the spleen and a history of endocarditis. Splenectomy is the treatment of choice and cure is obtained even in severe anaemic and septic conditions.

In haematogenous splenic abscess two types must be differentiated, namely, large septic infarcts after endocarditis and miliary abscesses after septicaemia or from peripheral foci. Aortography permits roentgenological diagnosis of large septic infarcts. Intra-aortic injections are recommended for the treatment of the miliary form.

Santos, R. dos (1939) *Pr. med.*, **47**, 1539

Chronic Splenic Enlargement (Chronic Splenomegaly)

Splenomegaly after Malaria

Treatment with acaprim. - I. Radvan describes 5 cases of enlarged spleen after malaria in which specific treatment with acaprim (a methyl-sulphomethylate of urea-6-aminoquinoline) was of no avail. Acaprim is described as having a specific action in the proplasmosis of domestic animals. The author used it in quantities of 1 mg. per kilo body weight, administered either subcutaneously or intramuscularly. 2 to 5 injections in aqueous solution are given at intervals of 2 to 3 days. The substance has an action similar to adrenaline with a strong action on the autonomic nervous system. It has an effect on the contraction of the spleen via the capillaries, but the mechanism of this contraction does not seem to be quite clear. It is not dangerous, but heart diseases, hypertension, diabetes mellitus, hyperthyroidism, and lung diseases are contra-indications.

Radvan, I. (1939) *Pr. méd.*, **47**, 1143

Tuberculosis

L. Howells reported 3 cases of tuberculous splenomegaly, one simulating Hodgkin's disease and the other two splenic anaemia. The first case was that of a woman of 55 years who bruised easily and suffered from loss of weight, dyspnoea and fatigue. The spleen was enlarged, a blood-count showed anaemia; later profuse vaginal haemorrhage, which was stopped by radium, and then ascites occurred. Splenectomy, when her general condition had improved under treatment, showed tuberculosis of the spleen and tuberculous masses in the stomach and liver. Ten years later the patient is alive and well. The second patient was a woman, aged 33, with the signs and symptoms of Banti's disease. It was found that the portal and

splenic veins were obstructed by adhesions from tuberculous peritonitis. Because of the adhesions the spleen could not be removed and it is doubtful if it was tuberculous. The anaemia responded to iron therapy but the patient died 13 years later from haematemesis. The third patient, a male aged 18, had had generalized enlargement of the lymphatic glands for 7 years. The liver and spleen were also enlarged. Biopsy showed that the glands were tuberculous and not those of Hodgkin's disease. Death was due to miliary tuberculosis. Howells stated that splenic tuberculosis is not rare. The diagnosis can usually be made because of associated tuberculous lesions. Splenectomy is the treatment of choice.

Howells, I. (1939) *Brit. J. Tuberc.*, **33**, 178

SPRUE, TROPICAL

See also B I M P, Vol. XI, p. 419

Aetiology

Endocrine Disturbances

J. Bauer writes on the frequency of the association of sprue with endocrine disturbances, and reports the case of a woman, aged 52, with sprue and premature senility. The glucose-tolerance test showed a very flat curve, a well-marked tendency to a secondary hypoglycaemic reaction, and a greatly increased sensitivity towards insulin; these reactions occur in anterior pituitary and in adrenal insufficiency, though the marked premature senility is more common in pituitary deficiency. The case must be differentiated from anorexia nervosa, which is psychological in origin; this is best done by a study of the patient's personality, and by settling the true time relation between the onset of symptoms due to pituitary deficiency and the failing nutrition. Another point to bear in mind is that the manifestations of anorexia nervosa are not always constant or identical. This case was regarded as one of pituitary dysfunction, which in such cases acts on the hypothalamic centres. It may be curable, since it is reversible, but it may also be fatal. This patient also had a low blood-calcium, but did not develop tetany. The hypocalcaemia was due to deficient absorption from the intestinal tract. Bauer and Jung had concluded that it is not the low blood-calcium that causes tetany, but the lack of calcium in certain parts of the central nervous system. This would explain the absence of tetany in this case.

Bauer, J. (1939) *J. trop. Med. (Hyg.)*, **42**, 245

and Jung, A. (1937) *Rev. Clin., Paris*, **75**, 284.

Treatment

Nicotinic acid

I. Justin-Besançon *et al.* report a case of tropical sprue which has been much ameliorated by nicotinic acid treatment. The patient, a male aged 56 years, had shown symptoms of the disease 2 years before he was admitted to hospital. He had the typical symptoms of sprue, namely, fatty diarrhoea, asthenia, oedema of the lower extremities, aphthae, stomatitis, and anaemia. The patient was first treated dietetically (raw apples according to the method of Moro), this gave only little relief. Then vitamin D, calcium, kaolin, and sulphanilamide were given without any constant improvement. The patient left hospital, but returned a short time later with symptoms of atrophy of the muscles of the lower limb and abolition of the reflexes. The total amount of lipoids in his blood was 1.75 g. per 1,000 g.; cholesterol 0.71 g. per 1,000 g., and calcium 75 mg. per 1,000 g. His stools contained 28 per cent of fat. Treatment with liver extracts improved his condition and weight, reduced the amount of lipoids in the blood, and caused the reflexes to reappear.

The patient then left hospital again but stopped taking the liver extract. He returned after 9 months in a very poor condition. He was then treated with nicotinic acid. He received a total of 1 g. of nicotinamide (nicotinic acid amide) intramuscularly in 3 doses, but without much improvement. He next received injections of liver extract, also without much improvement. Then he was given 1.5 g. of nicotinic acid in three doses each of 0.5 g. Improvement followed very rapidly and

after 10 days the patient was completely normal. Nicotinic acid was given again in doses of 0.15 g., 0.2 g., 0.25 g. and again 0.25 g., after which the fat disappeared from his stools.

Justin-Besançon, L., Caroli, J., and Inbona, J. M. (1936) *Bull. Soc. méd. Hôp., Paris*, **55**, 1135

STERILITY

See also B. E. M. P., Vol. XI, p. 447, Cumulative Supplement, Key Nos. 1455-1457, and Surveys and Abstracts 1939, pp. 30, 157 and 548

Sterility in the Male

Sperm Examination

O. J. Pollák and C. A. Joel explained the proper examination of semen to test the fecundity of the male. Before taking the sample, a full family, sexual, and medical history should be taken from both parties. A clinical examination, particularly of the primary and secondary sex characters should then be done. The semen should be collected 4 to 7 days after the last ejaculation and examined within 30 to 60 minutes. The quantity is normally 3.3 c.cm., less being pathological, and the consistency gelatinous. A change of colour or smell occurs only under pathological conditions. The sperms should then be counted, centrifuging or concentrating the specimen if necessary, and their motility observed, stimulating it with isotonic magnesium salts if necessary. The resistance of the sperm to hypertonic and isotonic acid and alkaline solutions should be determined. The specimen should be stained and the morphology of the sperms and the histology of the cells examined. By this method diseases and degenerations of the testicle and epididymis can be determined as well as the presence and function of the spermatozoa.

Effect of Diathermy on Testicular Function

J. Bauer and G. Gutman report on the effect of diathermy on testicular function in 5 cases of disturbance of the sexual function without evidence of somatic origin. Although in some of the cases there was subjective evidence of successful results, in all cases necrospemia, which had not been previously present, followed this treatment; this was ascribed to the diathermic heating of the organ, and disappeared about 10 to 14 days after cessation of treatment. Whether or not the endocrine function of the testes is increased by diathermy could not be settled by the available evidence. There was no doubt, however, that diathermic heating of the testes seriously affected spermatogenesis and consequently the *potentia generandi*. In view of the serious, though temporary, damage to spermatogenesis produced by diathermy, the authors do not recommend the method.

Effect of Sulphanilamide on Spermatogenesis

N. J. Heckel and C. G. Hori report on an examination of the semen of 11 men before and after giving sulphanilamide to see if it had any effect upon spermatogenesis. The sulphanilamide was given by mouth in doses of from 400 to 800 grains, over periods ranging from 16 to 58 days. They found that the drug had no effect upon the total number or the percentage of live spermatozoa.

Relation of Seminal Findings to Fertility

G. I. Moench considers the relation of seminal changes to fertility, with special reference to sperm concentration and the significance of testicular epithelial cells in the semen. The number of spermatozoa produced ordinarily is greatly in excess of that needed to fertilize the ovum, the author stated that he found 100,000 per c.cm. to be the average. A very great reduction in this number may occur before actual sterility occurs. Very long, tapering and narrow sperm heads are of particularly serious significance, and their shortening is often the first sign of improvement. Large numbers of cells from the tubular epithelium of the testes are present in abnormal cases.

Treatment

Gonadotrophic hormones.—R. S. Hotchkiss reports on the use of gonadotrophic hormones on the husband in 3 cases of sterile marriage, presumably due to deficient

spermatogenesis. In two cases injections of 10 units of anterior pituitary extract and 100 units of extract of pregnancy urine were given to the husband on alternate days for 106 and 90 days respectively. In the first case the number of spermatozoa per c cm. of seminal fluid rose from 2,000,000 to 8,500,000, and in the second case from 1,800,000 to 51,000,000. In both cases pregnancy occurred. In the third case 20 injections of 100 units of anterior pituitary extract and 500 units of extract of pregnancy urine were given on alternate days. The spermatozoa count rose from 6,000,000 to 73,000,000 per c cm., though no pregnancy had resulted up to the time of the report.

- Bauer, J., and Gutman, G. (1940) *Urol. cutan. Rev.*, **44**, 64.
 Heckel, N. J., and Hori, C. G. (1939) *Amer. J. med. Sci.*, **198**, 347.
 Hotchkiss, R. S. (1940) *Amer. J. Surg.*, **47**, 45.
 Moench, G. L. (1940) *Amer. J. Surg.*, **47**, 586.
 Pollák, O. J., and Joel, C. A. (1939) *J. Amer. med. Ass.*, **113**, 395.

Sterility in the Female

Treatment

Tubal insufflation—According to H. Violet insufflation of air into the uterine (Fallopian) tubes (Rubin's method) is the method of choice in the treatment of sterility in the absence of venereal disease. Injection of lipiodol defeated its own object by producing in a number of cases a sterile inflammation which caused further adhesions, cysts, and even local peritonitis. Tubal insufflation should be performed one week after menstruation has ended, as the swollen state of the mucosa of the uterus and tubes at an earlier stage may lead to failure.

Violet, H. (1939) *Monde méd.*, **49**, 699.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

See also B.F.M.P., Vol. XI, p. 476, Surveys and Abstracts 1939, p. 549.

Malignant Tumours

Carcinoma

Gastric secretory depressant principle.—A. Brunschwig *et al.* previously reported their finding that, when samples of achlorhydric gastric juice from patients with pernicious anaemia were injected intravenously into dogs with gastric pouches which had been stimulated by feeding the animals, a transitory depression of pouch secretion and achlorhydria occurred. They concluded that in pernicious anaemia there might be an excess of a gastric secretory depressant in the stomach. The authors now report the effect of intravenous injection into dogs with stimulated gastric pouches of achlorhydric gastric juice from patients with carcinoma of the stomach in order to test for the presence of a gastric secretory depressant action. Of 27 samples, 21 were found to exert an inhibitory action on the pouch secretions, as compared with 16 out of 80 samples regarded as controls, from patients either free from carcinoma of the stomach, or with carcinoma but normal acid secretion or hyperchlorhydria. The depressant factor considered to be present was inactivated by boiling the juice containing it for 10 minutes.

Diagnosis and Differential Diagnosis

Phenolphthalein test.—B. M. Banks and L. E. Barron employed the diagnostic phenolphthalein test on 52 patients with intrinsic lesions of the gastro-intestinal tract, malignant and non-malignant, and on 151 controls with a variety of other conditions or with no demonstrable organic disease. In 25 per cent of the cases with proved disease of the alimentary tract the test was negative, and in one-sixth of the control cases the test was positive. The authors concluded that the test had too wide a range of error to be considered reliable in the diagnosis of gastro-intestinal disease.

Early radiological diagnosis of gastric carcinoma. In the 21st Silvanus

Thompson Memorial Lecture on Recent Advances in the Röntgen-Diagnosis of Gastric Cancer, R. Ledoux-Lebard of Paris sets out his conclusions from very numerous cases, followed from the combined clinical and radiological aspects, of the various forms, sites, and manifestations of primary neoplasms of the stomach. Stress is laid on the impossibility of making an early correct diagnosis on clinical grounds alone, and on the occurrence of cases running a prolonged course. In one dramatic instance a radiological diagnosis of cancer of the lesser curvature was made, but at laparotomy the surgeon could not see or feel any such lesion and therefore firmly refused to go any further or remove any part of the area indicated. more than 3 years later the patient was again operated upon and died in a few months with generalized metastases. Quite clear conclusions are drawn about the diagnosis between the innocent and malignant nature of gastric ulcers. It is now possible to recognize among the various radiological pictures of ulcerative lesions, mainly of niches, some forms that show a continuous evolution and a constant, if sometimes very slow, progress whatever the treatment adopted, until they reach a stage when they force a diagnosis of cancer. The dictum, however, that 'the larger the niche the more suspicious it should be, and if its size exceeds 3 cm., it is almost certainly cancerous' is often misleading, the size is more important than the size of the niche. Thus ulcers in the vertical part of the lesser curvature hardly ever become malignant, for in this position primary carcinoma of the ulcerative type is the usual form, whereas in the horizontal part of the lesser curvature even small ulcers often show carcinomatous transformation. Instead of being regarded as necessarily a tumour, gastric cancer should also be recognized as an infiltration or as an ulceration, both of small size, sometimes visible only with the aid of a magnifying glass. The well-known meniscus sign is seldom present at a very early stage.

From benign ulcer—W. L. Palmer held that the existence of carcinomatous degeneration in benign gastric ulcers remained to be conclusively proved. On the other hand peptic ulceration of carcinoma might produce a lesion indistinguishable from benign ulcer, unless examined microscopically. While there is no pathognomonic sign which indicates the benign nature of a gastric lesion, a careful correlation of clinical signs, symptoms, and history can differentiate benign and malignant ulcers with a high degree of accuracy.

Treatment

Total gastrectomy—J. M. Waugh and H. B. Neel reported 2 cases in which complete gastrectomy had been performed for carcinoma of the stomach. Both are alive and in good health, one 13 and the other 6 months after operation. The latter case was reported in detail. A woman of 68 years was found on operation to have a completely leather-bottle stomach. She had had dyspepsia for years and before operation a movable mass was felt above the umbilicus. The stomach was freely movable, there were no distant metastases, and the patient's general health was considered good enough to withstand so major a surgical procedure. The entire stomach, with the gastrocolic and gastrohepatic lymph nodes and ligaments, was removed. The duodenum was closed and planted into the head of the pancreas. The jejunum was sutured to the oesophagus. Entero-anastomosis was made between the 2 limbs of the jejunum and a tube was passed down the nose through the 2 regions of anastomosis into its distal limb. Intravenous fluids were given during the operation. Skimmed milk, every hour, was given through the nasal tube on the 4th post-operative day. Water was given on the 9th day and gradually cereals, ice-cream and milk drinks were added. On the 16th day the tube was removed and the patient had a bland diet. On the 23rd day she left hospital. Since then her weight and appetite have improved and she feels very well. A cough after the operation led to a suspicion of pneumonia. The presence of the nasal tube enabled sulphapyridine to be given with success.

- Banks, B. M., and Barron, L. I. (1939) *New Engl J Med.*, **221**, 296.
 Brunswick, A., Clarke, T. H., van Prohaska, J., and Schmitz, R. I.
 (1940) *Surg. Gynec. Obstet.*, **70**, 25.
 Ledoux-Lebard, R. (1940) *Brit J Radiol.*, N.S., **13**, 37.
 Palmer, W. L. (1939) *Ann intern Med.*, **13**, 317.
 Waugh, J. M., and Neel, H. B. (1940) *Proc. Mayo Clin.*, **15**, 54.

Foreign Bodies in the Stomach*Diospyrobezoar*

D. C. Browne and G. McHardy report a case of diospyrobezoar in the stomach. Examination by a Wolfe-Schindler flexible gastroscope showed a foreign body, greyish-black, irregular in outline, glistening and covered with mucus; this was removed at operation, but the patient died some days later of pneumonia. At necropsy there was an ulcer 2.5 cm. in diameter on the lesser curvature.

Browne D. C., and McHardy, G. (1940) *Arch. intern. Med.*, **65**, 368.

STRABISMUS

See also B.F.M.P., Vol. XI, p. 492; and Surveys and Abstracts 1939, pp. 131 and 551.

Latent Squint*Heterophoria*

New tests—F. H. Verhoeff described new tests for hyperphoria. He defined heterophoria as a tendency for the eyes to deviate with respect to each other during binocular fixation. He pointed out that the usual tests such as the Maddox rod do not measure the direction and amount of the heterophoria during binocular fixation, but during its absence. He therefore designated this factor presumptive heterophoria. Heterophoria can be divided into its horizontal and vertical components. It is possible to exclude all stimuli to vertical binocular fixation while retaining these to horizontal fixation by means of a target with vertical lines only of such size that it extends beyond the limits of the binocular visual field. A smaller, more practical target may be used by restricting the eye to the central half of the field by the use of an iris diaphragm. Two small holes are pierced horizontally in the middle of the target with a vertical white line between them. They are illuminated so that the hole on the right is seen by the right eye only and the other by the left eye only. At the proximal end of a long tube a prism producing a maximal deviation of 15 prism diopters is mounted. The patient sits 6 metres from the target and manipulates the prism until the two holes appear horizontal. The amount of hyperphoria is then read from the amount of rotation of the prism. Stereopsis can be used as the indicator in another test in which the patient rotates the prism until he brings the arc of a circle in the same plane as two vertical lines. Verhoeff has found these tests of practical value in the treatment of hyperphoria.

Verhoeff, F. H. (1939) *Arch. Ophthalm., N.Y.*, **22**, 743.

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

See also B.E.M.P., Vol. XI, p. 503; and Surveys and Abstracts 1939, pp. 121 and 552.

Child-birth after Presacral Neurectomy

I. V. Pearce reports the case of a woman, aged 25, who in January, 1937, underwent presacral neurectomy for dysmenorrhoea, and in December, 1938, gave birth to a male baby weighing 8½ lb., after a quick and easy labour. Two previous pregnancies had ended in prolonged and difficult labours. The operation resulted in cure of the dysmenorrhoea, it had not any adverse influence at any stage of the pregnancy, and it appeared to have been a factor in producing the easy and quick labour for the third child.

Pearce, T. V. (1940) *Brit. med. J.*, **1**, 87.

SYPHILIS

See also B E M P., Vol. XI, p. 526; Cumulative Supplement, Key No. 1467, Surveys and Abstracts 1939, pp. 151 and 553; and p. 87 of this volume

Laboratory Tests*Comparison of the Wassermann and the Meimicke Flocculation Tests*

J. C. Thomas quotes Nicole and Fitzgerald's assumption in 1932 that the Wassermann complement-fixation test had at last paused to rest in the limbo of historically interesting experiments, but brings forward statistical evidence to prove that there is not any reason to abandon the Wassermann reaction in sole favour of the Meimicke (M K R II) flocculation tests in the diagnosis of syphilis. Since 1934 all new admissions to the Middlesex County Mental Hospital, Shenley, have been tested by the Wassermann and Meimicke methods. An elaborate analysis of 3,284 parallel cases shows that they agreed in 97.9 per cent and after adjustment in 98.5 per cent. A new Meimicke method, described by W. M. Ford Robertson and D. B. Colquhoun (1939) was employed in 482 cases; the correlation between this (M K R (F R C.)) and the Wassermann test with serum was of the same degree as with the original Meimicke reaction. W. M. Ford Robertson appended a note to Thomas's article.

Serum Tests

Modified Kolmer test. J. A. Kolmer reported a further simplification of his complement-fixation test for syphilis. He stated that he believed that the serum diagnosis of syphilis should always rest upon 2 tests and that one of them should be a complement-fixation test. The test requires only 0.2 c.cm. of serum or 0.5 c.cm. of spinal fluid. The serum is heated to 55 to 56 °C. in a water-bath for 30 minutes. Two test-tubes are used, 0.5 c.cm. of saline being put in the control tube. Into each tube is put 0.2 c.cm. of serum, and 0.5 c.cm. of Kolmer C.I. antigen is added to the first tube only. After 10 minutes 1 c.cm. of complement is added to both tubes, which are then placed in a refrigerator at 6° to 8° C. for 15 to 18 hours. Following this the tubes are heated in a water-bath at 37 °C. for 10 to 15 minutes, then 0.5 c.cm. of haemolysin and 0.5 c.cm. of 2 per cent suspension of washed sheep's corpuscles are added to both tubes. The readings are then made. This test has the advantage that it can be done quickly and cheaply and is of special value in laboratories where a large number of tests have to be made.

Boerner-Lukens modification of Wassermann test. R. L. Gilman *et al.* report on the results obtained with the Boerner-Lukens modification of the complement-fixation test, which has recently been evolved by two of the authors. This test differs from other modifications of the Wassermann test particularly in the mixing of some of the reagents in bulk and in the use of optimal doses of complement, haemolysin, and antigen in place of units. Antigen and complement are combined and added as a single increment to the patients' serum, and then sensitized sheep's cells are added. All reagents are used in smaller amounts, i.e. 0.1 c.cm. of serum is used, 0.5 c.cm. of antigen-complement, and 0.5 c.cm. of sensitized cells. The total is slightly over 1 c.cm. The full technique was described by Boerner and Lukens in 1939. This test is held to simplify the use of an easily prepared antigen, and the addition of the reagents in combination. In the series of 1,500 tests there were 20 instances of lack of accord in specificity.

Boerner, F., and Lukens, M. (1939) *Amer. J. clin. Path.*, **9**, 13.
Gilman, R. L., Boerner, F., and Lukens, M. (1940) *Arch. Derm. Syph. (N.Y.)*, **41**, 32.

Kolmer, J. A. (1939) *Amer. J. clin. Path.*, **9**, 581.

Nicole, J. F., and Fitzgerald, E. J. (1932) *J. ment. Sci.*, **78**, 96.

Robertson, W. M. Ford, and Colquhoun, D. B. (1939) *J. ment. Sci.*, **85**, 548.

Thomas, J. C., and Robertson, W. M. Ford (1939) *J. ment. Sci.*, **85**, 1241.

Clinical Picture

Acquired Syphilis

Rupial syphilis—J. Thetford and J. L. Callaway record a case of a negress, aged 39, with rupial syphilis, a manifestation now rare. The skin condition first began as a small area of discrete circumscribed pustules on the left hand and forearm, and later appeared on the abdomen, they were painful and tender, measured from 1 to 3 cm. in diameter, did not itch, and discharged purulent material. They spread concentrically until almost the whole body was involved. After specific and local treatment the lesions ultimately healed without scarring, but with marked depigmentation.

Thetford, J., and Callaway, J. L. (1940) *Urol. cutan. Rev.* **44**, 306

Treatment

Early Acquired Syphilis

Massive-dose chemotherapy by intravenous drip—H. T. Hyman *et al.* treated early syphilis with massive-dose chemotherapy by the intravenous drip method. A 5 per cent dextrose solution was given at a rate of approximately 100 c.c.m. per hour. At the end of each hour 0.1 g. of neoarsphenamine dissolved in 50 c.c.m. of 5 per cent dextrose was added. This went on for 15 hours until a total dosage of 1 g. of neoarsphenamine had been given. The needle was kept *in situ* all day. The diet was semi-solid and rich in carbohydrates. Both primary and secondary lesions healed rapidly and dark-field examinations were negative within 24 hours. The patients were free from infectivity on discharge from hospital. The effect on the general health and well-being of the patient was good. There were many toxic effects in this series which could not be controlled by vitamin therapy. Febrile reactions, skin rashes, and one case of fatal haemorrhagic encephalitis occurred. The authors concluded that massive-dose chemotherapy in spite of its efficiency must be used with caution until some means has been found to circumvent these toxic reactions.

Mapharsen—L. Chargin *et al.* treated 188 cases of early syphilis with continuous mapharsen (mapharside) and bismuth. Male patients received maximal injections of 0.06 g. of mapharsen and females 0.04 g., the initial dose being 0.04 and 0.03 g. respectively. Those with sero-negative primary syphilis received 20 to 47 injections, those with sero-positive primary syphilis 20 to 56, and those with secondary syphilis 20 to 72. All patients received injections equal to, or greater in number than the arsenical injections of 1.5 c.c.m. of 10 per cent bismuth subsalicylate in oil. This series was compared with 169 cases of early syphilis similarly treated with arsphenamine or neoarsphenamine. The results of treatment with mapharsen were satisfactory in 84 per cent of cases. Most of the cases were observed for over 18 months and the rest between 12 and 18 months. The best results were obtained in the sero-negative primary stage and the worst in the sero-positive primary stage. There were only mild toxic symptoms in this series although 3 patients developed jaundice. They all recovered and were able to resume the treatment. Chargin *et al.* concluded that owing to its mild toxicity and ease of administration mapharsen deserves a further trial in the treatment of early syphilis.

Sobisminol mass—J. R. Scholtz *et al.* treated 5 cases of sero-positive primary syphilis, 27 cases of secondary syphilis, 12 cases of benign syphilis of the bones, skin and mucosa, 23 cases of syphilis of the central nervous system, and 23 cases of early and late latent syphilis with sobisminol mass by mouth. Nine capsules daily were given at the beginning of the treatment. This was not very well tolerated and was later reduced to 6 capsules, which were found to be adequate. Involution of the skin lesions of primary and secondary syphilis took slightly longer than in cases treated with neoarsphenamine. In the central nervous system cases, particularly tabetics, marked relief was obtained, greater than any other drug has given before. Most of the patients tolerated the drug well except for mild gastro-intestinal symptoms. The authors concluded that although sobisminol mass given by mouth is effective in the treatment of syphilis it has no greater therapeutic value than other forms of bismuth. Its advantage is that it is pleasant and easy to give, but

there is a serious disadvantage in that the regular taking of it depends on the honesty and care of the patient

Continuous plan of treatment - H. Orr described a plan of treatment of syphilis in which no rest periods were allowed. For sero-negative primary syphilis, prompt and adequate treatment will effect a cure in practically every case. The patient is given an intramuscular injection of neoarsphenamine, and an intramuscular injection of bismuth. The dose of the former is 0.45 g. for adult patients under 175 pounds, and 0.6 g. for heavier patients. The drug is repeated on the second and third days, and then every 5 to 7 days until a total of 10 injections has been given. At the same time the bismuth is given every 14 days, and, at the conclusion of the course of 10 injections of neoarsphenamine, the bismuth is given every 2 to 7 days, depending on the preparation, until 15 injections have been given. The second course is started at once, without any rest period, and is similar to the first course, except that the intensive treatment given on the first 3 days is omitted, the neoarsphenamine being given at 5- to 7-day intervals throughout. The spinal fluid is examined between the ninth and eleventh months, and Wassermann and van den Bergh tests are made at the time of every intravenous injection. If all 30 Wassermann tests and the spinal fluid have been negative, the patient is regarded as cured. He is, however, kept under observation for at least another 2 years, the Wassermann test being performed every 3 months. The treatment for sero-positive syphilis is exactly the same, except that the intensive treatment during the first 3 days is omitted. More than 2 courses are often necessary. Even though at the end of treatment the patient is free from symptoms, and the blood and cerebrospinal fluid are negative, the patient should be kept under observation indefinitely. In latent or late syphilis, to avoid a Herxheimer reaction, a preliminary 6 weeks' course of an insoluble bismuth salt should be given; 0.05 g. should be given intramuscularly on the first and fifth days, then 0.1 g. every 5 days thereafter. Neoarsphenamine may then be given as above. In both asymptomatic and symptomatic neurosyphilis malarial fever therapy should be used, unless contraindicated. This should consist of 10 chills with a pyrexia of not less than 105° F. Several courses of arsphenamine and bismuth are then given. Tryparsamide is most suitable.

Side Effects of Arsphenamine Treatment

G. C. Parker and O. C. Perkins reported 4 cases of arsphenamine poisoning. The authors advanced the hypothesis that, in the administration of arsphenamine itself, the dihydrochloride, which is strongly acid, there is first an agglutination of red-blood cells which results in minute emboli in the vessels of the brain and other special organs. After the administration of arsphenamine, the blood vessels may rupture in the stage of elevated pressure. This train of events seemed best to explain the occurrence of ring-haemorrhages. Patients with latent syphilis are more apt to develop reactions than those with early lesions. Young adults are probably more susceptible to the toxic effects of arsenical injections.

Liver injury modified by diet—Liver damage not uncommonly follows prolonged arsenical treatment of syphilis. It has been found that carbohydrates protect the liver from damage by chloroform; others have found fat and protein protective against liver toxins. W. J. Messinger and W. B. Hawkins gave arsphenamine to dogs and noted the effect of diet upon the hepatic damage produced. Protein was the best protector, then carbohydrate. Fat had a very bad effect. The fat-fed dogs became jaundiced, highly toxic, and in addition, dogs given carbohydrate or protein to protect them, if suddenly given fats instead, became more ill and jaundiced; this occurred even if arsphenamine was discontinued after the diet was changed. Similarly, jaundiced toxic fat-fed dogs could be protected from the action of arsphenamine by the administration of protein or carbohydrates. As long as they continued on the latter diet injection of arsphenamine did not produce toxic results.

Side effects of mapharsen on liver.—I. Snapper *et al.* described the case of a man, aged 22, who developed jaundice, followed within a week by symptoms of acute liver insufficiency and death after 4 months of antisyphilitic treatment with neoarsphenamine (total amount 7.4 g.), bismuth sodium salicylate (total 1.3 g.), and one last mapharsen injection of 0.03 g. At necropsy the liver was found to be moderately enlarged, and weighed 2,080 g. The capsule was smooth and tense. The liver

tissue was greenish-yellow, and mottled all over with deep red spots. Microscopically extensive destruction of liver cells with marked infiltration in the portal spaces was found. The case was remarkable in that the liver remained large to the end in spite of the fulminating course of the condition. The authors considered that the mapharsen may have aggravated the condition of the liver, and advised that mapharsen should not be given in cases of arspenamine hepatitis.

Side Effects of Bismuth Therapy

Cervico-vaginitis.—C. Simon (1933) reported a case of cervico-vaginitis due to bismuth and he now describes another case of a patient who had bismuth injections for syphilis. There was nothing remarkable about the patient except that the cervix and vagina were very lately healthy. After two months she acquired a bismuth stomatitis and the author discovered at the time that the cervix was covered with a grey adherent false membrane. The next day she has a profuse bleeding from the cervix which was now oedematous and covered with ulcers. The ulcers extended in a few days' time to the vagina. Characteristic of this disease are the blue-black spots on the vagina. There is no fever and the blood picture is normal.

Chargin, I., Leifer, W. and Rosenthal, T. (1939) *Arch. Derm. Syph. N. Y.*, **40**, 208.

Hyman, H. F., Chargin, I., Rice, J. L., and Leifer, W. (1939) *J. Amer. med. Ass.*, **113**, 1208.

Messinger, W. J., and Hawkins, W. B. (1940) *Amer. J. med. Sci.*, **199**, 216.

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Simon, C. (1933) *Ann. Derm. Syph., Paris*, p. 193.

(1940) *Pr. med.*, **48**, 351.

Snapper, I., Chin, K. Y., and Liu, S. H. (1939) *Chin. med. J.*, **56**, 501.

TLSTIS AND CORD DISEASES

See also B L.M.P., Vol. XI, p. 656, and Surveys and Abstracts 1939, p. 559

Compensatory Testicular Hypertrophy after Unilateral Orchidectomy

H. A. Zide reviews the question whether or not compensatory hypertrophy of the remaining human testis occurs after unilateral orchidectomy or atrophy. He examined 19 adult patients in whom unilateral testicular abnormality had occurred after puberty. Owing to the rarity of orchidectomy or atrophy in childhood pre-pubertal clinical material was not available, but a review of recent reports did not mention compensatory hypertrophy of the testis before puberty. Unilateral cryptorchidism, as seen at the Mayo Clinic, has not resulted in an appreciable hypertrophy of an opposite normally placed testis.

According to reports on animals by various observers, compensatory hypertrophy after unilateral castration does not occur in immature and mature mice; in dogs and guinea-pigs, some authors have reported hypertrophy and others no change. The rabbit is the only experimental animal in which all observers have found hypertrophy, varying from 15 per cent to 100 per cent increase by weight.

In the group of the 19 adult patients at the Mayo Clinic, 17 had developed unilateral atrophy after mumps orchitis and in the remaining 2 orchidectomy had been performed. The length and width of the unaffected testis were measured with callipers. The testes of a control group of 29 normal adults were also measured. The size of the testes of the control series averaged 3.8 cm. in length by 2.3 cm. in width, these measurements comparing fairly closely with published figures for normal adults. The remaining testes of the 19 patients with one absent testes averaged 3.9 cm. in length by 2.5 cm. in width. The difference in size between the two groups was not significant in view of the small number of cases studied; but so far as it goes this study did not support the suggestion that the adult human

testis undergoes any appreciable compensatory hypertrophy after atrophy or removal of the other testis.

Zide, H. A. (1939) *J. Urol.*, **42**, 65.

Diseases Arising from Interference with Blood-Supply

Infarction

Infarction of the testis not associated with torsion of the spermatic cord is very uncommon. J. G. Menville reports a case occurring in the right testis of a man aged 26 years. He had previously had mumps complicated by orchitis. Pain developed in the testis during coitus. It gradually increased in severity. There was no history of trauma or gonorrhoeal or other infection. The epididymis was not implicated. As the pain became worse the testis became hot and the patient's temperature rose. A leucocytosis developed, orchidectomy was performed, and showed an infarct due to thrombosis of the arteries supplying its middle third.

Menville, J. G. (1940) *J. Urol.*, **43**, 333

Tumours

M. B. Wesson reviewed the histories of 7 malignant tumours of the testes, 4 being seminomas, 2 malignant teratomas, and one a testicular cyst simulating a teratoma. Two cases survived after operations which were performed more than 15 years previously, but one patient died from metastases within 75 days of the teratoma first being noted. The author did not look upon trauma as a causative agent, but merely as something directing the patient's notice to the swelling. He considered that the best treatment for these tumours is orchidectomy followed by deep X-ray therapy. Operation should be prompt, in view of early metastases, and preferably should be preceded by maximal deep X-ray therapy, as soon as the patient is admitted to hospital.

Wesson, M. B. (1939) *Brit. J. Urol.*, **11**, 338

TESTIS, UNDESCENDED

See also B1 M.P., Vol. XI, p. 671, Cumulative Supplement, Key No. 1480, Surveys and Abstracts 1939, p. 561, and p. 14 of this volume.

Treatment

Gonadotrophic Substance

Psychological effects—I. Davidoff reported the psychological effects of treatment in 21 cases of cryptorchidism, 11 of which were bilateral, 2 unilateral, 3 scrotal and 5 pseudo-cryptorchid. Antuitrin-S (chorionic gonadotrophin), in doses of 100, 200, or 300 units once or twice a week intramuscularly, and autophysin were given to the patients. Of the 13 true cryptorchids only 3, or 23 per cent, gained descent of the testicle. All three pairs of scrotal testes assumed a more normal position. In the whole series descent occurred in 11 cases only, or 52 per cent. The results were better in the pseudo- than the true cryptorchids. The mental behaviour of the patient could not be ascribed to the cryptorchidism alone, and there was no correlation between descent of the testicles and improvement in the mental state.

Surgical

N. S. Moore and S. M. Tapper believe that the reason why a testis does not migrate down to the scrotum is due primarily to the thickness of the cremasteric fascia forming bands of adhesions along its course and holding back the testis, the gubernaculum probably does not produce traction on the testis, but serves as a guide for its migration. They employ a modification of the Torek operation in cases of undescended testis. After the testis has been brought down to the scrotum, it is anchored to the thigh with linen sutures for 2 weeks, it is also anchored to the bottom of the scrotum with catgut sutures. A purse-string chromic suture in the superficial fascia around the cord in the superior portion of the scrotum, by producing a band of adhesions, prevents the testis from subsequently slipping back to its original position. Employment of this method has not in the authors' experience

been followed by atrophy of the testis, or infection, or sloughing of the parts in the 7 years in which it has been used.

Davidoff, F. (1940) *J nerv ment Dis.*, **91**, 724

Moore, N. S., and Tapper, S. M. (1940) *J Urol*, **43**, 204

TETANUS

See also B I M P, Vol. XII, p. 1, Cumulative Supplement, Key No. 1481, Surveys and Abstracts 1939, p. 562, and pp. 10 and 137 of this volume.

Treatment

Prophylaxis

I. Jaeger discusses the point of view of Boehler and Ehalt who say that if there is a proper excision of wounds no further tetanus prophylaxis is necessary. Boehler had stated that, in very dirty wounds, where for some reason or other no excision of the wound was made, serum prophylaxis should be carried out. The author, after enquiries in all German University hospitals, came to the conclusion that every fresh wound should be excised, and that a wound should be treated with tetanus antiserum if it cannot be made free of germs through excision due to its size or if it is dirty. Excision and injection should be made as early as possible. There has been no case of tetanus in the author's hospital where they adhere strictly to these rules. There have been seven cases of tetanus in Boehler's clinic in patients where the excision could not be carried out completely, and where no serum injection was made. This leads to the conclusion that Boehler's treatment is incomplete.

Active immunization—H. Gold found that 2 injections of tetanus alum-precipitated toxoid caused a higher level of antitoxic immunity than 3 injections of plain toxoid or plain toxoid with the addition of 0.4 per cent alum. The loss of antitoxin is most marked in the first few months following basic immunization, with the result that the minimal level of 0.1 unit of antitoxin per c.cm. of blood serum is not usually maintained for more than a year. To counteract this, at the time of the injury, a further dose of toxoid is administered, and thus brings the antitoxin level, in a patient previously immunized, to 0.1 unit within 4 to 6 days; the plain toxoid is perhaps more rapid in its action than the precipitated. One week after this dose, the antitoxin titre of an immunized subject is between 2 and 50 times greater than the titre produced by the injection of 1,500 units of tetanus antitoxin. Though there is a fall in this figure, the loss is much more gradual than that following the primary injections.

Anaphylaxis after tetanus toxoid—H. F. Whittingham reported 2 cases of anaphylactic shock following the injection of a second dose of tetanus toxoid. In both cases the patient gave a positive skin reaction to Witte's peptone. The author reviewed 61,042 members of the Royal Air Force immunized by the two-dose method of giving tetanus toxoid, 1 c.cm. at 6-weekly intervals, and found that 14 cases (0.023 per cent) showed definite constitutional symptoms such as frontal headache and pains in the body and limbs with slight pyrexia; of these, 2 cases had immediate anaphylactic crises. Local reactions only, consisting of stinging in the inoculated area, itching, urticaria, etc., occurred in 651 cases (1.06 per cent).

H. J. Parish and C. I. Oakley also reported a case of anaphylaxis occurring in a woman a few minutes after a second injection of 1 c.cm. of tetanus toxoid. The manifestations were marked flushing of face and hands, severe abdominal pain, intense desire to micturate, severe backache, swelling of lower lip, incoherent speech, and urticarial wheals. These phenomena, though alarming, are rare after tetanus toxoid, and appear to be due to some constituent of the medium in which tetanus toxoid is prepared, possibly the Witte peptone. Adrenaline, 1 in 1,000, should be readily available as a precautionary measure, when tetanus toxoid is injected.

R. A. Cooke *et al.* reported a case of generalized urticaria in a man given a second injection of tetanus toxoid. They suggest the following measures as a means of preventing such allergic phenomena. A scratch test should always be made before the second, or any later, injection of toxoid preparations. If the test is definitely positive, the injection should be postponed, and the test repeated in from 4 to 6 months. If the reaction is slight the second dose should be given cautiously in small

fractions, beginning with 0.2 c.c. of a 1 in 10 dilution of the toxoid, then after 20 minutes if no reaction 0.5 c.c. of the dilution; then, after a further 20 minutes, 0.1 c.c. of the concentrated toxoid. Adrenaline solution should be kept at hand for immediate use.

- Cooke, R. A., Hampton, S., Sherman, W. B., and Stull, A. (1940)
J. Amer. med. Ass., **114**, 1854.
 Gold, H. (1939) *Ann. intern. Med.*, **13**, 768.
 Jaeger, F. (1939) *Schweiz. med. Wschr.*, **69**, 735.
 Parish, H. J., and Oakley, C. L. (1940) *Brit. med. J.*, **1**, 294.
 Whittingham, H. F. (1940) *Brit. med. J.*, **1**, 292.

TONSILS DISEASES

See also B.E.M.P., Vol. XII, p. 40, and Surveys and Abstracts 1939, p. 563

Bacteriology

L. V. Keogh *et al.* investigated the serological groups and types of streptococci isolated from 378 pairs of tonsils excised in the Children's Hospital in Melbourne. Of these 259, or 68.5 per cent, contained haemolytic streptococci, 189, or 50 per cent, of them belonged to Group A, 21, or 5.5 per cent, to Group B, 33, or 8.7 per cent, to Group C, and 28, or 7.4 per cent to Group G. A small but similar examination carried out on tonsils removed in a private hospital gave the same results. In 12 cases two different strains were present, Group A being one of them in 11 instances. In 466 throats of healthy children and adults Group A haemolytic streptococcus was found in 4.5 per cent only. The clinical indications for tonsillectomy are, therefore, supported by the bacterial findings in about 33 to 50 per cent of the cases. It is definitely stated that this article is not a panegyric for routine tonsillectomy. An examination of the bacteriological flora of acute and chronic infections of the maxillary sinuses in 100 cases showed that haemolytic streptococci were found in 5 cases, and of these 5 there were 2 only of Group A, this makes it improbable that sinus infections account for the high rate of Group A haemolytic streptococci on inflamed tonsils.

- Keogh, F. V., Macdonald, I., Battle, J., Simmons, R. T., and Williams, S. (1939) *Brit. med. J.*, **2**, 1036.

Enlarged Tonsils and Adenoids

From observations during 25 years of 1,136 cases of enlarged tonsils and adenoids in the Peterborough district, C. Rolleston draws the following conclusions: the condition is commoner in boys (55 per cent) than in girls (45 per cent), and in both sexes between the ages of 4 to 8 years. The method of upbringing in infancy—breast or bottle feeding—has not any aetiological importance, but there is an inherited disposition to the disease. Deafness is more than 16 times commoner in these patients than among controls. There is a definite relation between excess of dental caries, i.e. a mouth with more than 4 carious temporary or permanent teeth, and enlarged tonsils and adenoids, among the 1,136 patients excessive caries was present in 470, or 41.3 per cent, as compared with 944, or 24 per cent, among 3,944 controls. The patients are not more prone to rheumatism than are controls. The patients showed enlarged glands at the angle of the jaw in 54 per cent. Enlargement of the thyroid, which is very common in the Peterborough area, occurred in 4 per cent of the patients. Enlarged tonsils and adenoids cause considerable retardation in education, and their removal is one of the most successful of all operations. The text contains a commentary of current opinion.

- Rolleston, C. (1939) *Brit. J. Child. Dis.*, **36**, 251.

Removal of Tonsils

Effects on Surrounding Tissues

L. H. Campbell investigated the effects of tonsillectomy on surrounding tissues, and its local results, in 621 girl students between the ages of 18 and 21 years. Of

these 77.3 per cent showed tonsillar remnants in the fossae, and in 10.6 per cent of them the remnants were infected. In 153 of this series there was in 54.9 per cent an excessive amount of lymphoid tissue in the pharynx, and on 22.8 per cent scarring of the palate, pillars, or fossae. The percentage of tonsillar remains was about the same whether the patient had been operated on by a specialist or by the family practitioner. The author stated that these remnants were usually due to incomplete operation, some tonsillar tissue at the lower pole usually being left behind. The recurrence may be due to hyperplasia of local lymphoid tissue. Scarring was much more frequent after operations not performed by specialists. Recurrent tonsillar tissue often causes symptoms and by forming a focus of infection may give rise to more trouble than did the original tonsil.

Campbell, F. H. (1939) *Arch. Otolaryng.*, Chicago, **30**, 863.

TOXICOLOGY: HOMICIDAL, SUICIDAL, AND ACCIDENTAL POISONING

See also B. E. M. P., Vol. XII, p. 59, Cumulative Supplement, Key Nos. 1491-1527, and Surveys and Abstracts 1939, p. 565.

Gases

Carbon Monoxide

B. Wollek records a rare case of carbon monoxide poisoning in a boy aged 12. Temporary amaurosis developed, but cleared up a fortnight after treatment was begun. The author discusses the 2 distinct stages of carbon monoxide poisoning: (i) the prodromes of which are headache, vertigo, cough, excitability, lassitude, onset of muscular palsy, and (ii) finally a state of complete paralysis, starting with sensory paralysis and ending with complete motor paralysis, though muscular spasms often occur. The second stage develops a few days after intoxication or even later and is characterized by localized effects of ischaemia, such as muscular gangrene, dermatitis, peripheral neuritis, pemphigus, headache, and nervous conditions resembling Parkinsonism and disseminated sclerosis. The present case showed, instead of any of the above symptoms, sudden amaurosis which, however, cleared up with persistent oxygen, blood transfusion, and betaxin.

R. B. C. Thomson reports a case of chronic exhaust-gas poisoning in a man, aged 30, who constantly drove a car and began to suffer from gastro-intestinal discomfort, nausea, anorexia, and headache. This was first thought to be due to a peptic ulcer, but 6 weeks later there was not any radiological evidence of ulceration, though the symptoms still persisted. He was anaemic. While the car was out of use in the winter the symptoms disappeared, but returned when the car was again used. Examination of the car showed that there was a flaw in the exhaust apparatus, and when this was corrected, the symptoms did not recur.

Thomson, R. B. C. (1940) *Canad. med. Ass. J.*, **42**, 464.

Wollek, B. (1939) *Arch. Kinderheilk.*, **117**, 257.

Synthetic Organic Substances

Acetanilide

A. Leslie reported a case of acetanilide poisoning. Two types of such poisoning occur, acute and chronic. He reported an acute case in a patient who had taken as many as 15 to 20 'bromo-seltzer' drinks a day for the relief of a migrainous headache. Each dose contained approximately 0.24 g. of acetanilide. The patient vomited and his temperature rose to 103° F. He became semi-comatose, disoriented, and very cyanosed. The pupils were equal and reacted, there was bilateral nystagmus, intention tremor, and hyperactive deep reflexes. The urine was very dark. On withdrawal of the drug and administration of copious fluids the patient improved and rapidly recovered. The headache also disappeared. The cyanosis is probably due to the presence of methaemoglobin or sulphaemoglobin. Although the drug is a good analgesic, continued use may produce headache, as in this case. Tolerance to the drug is rapidly established.

Naphthalene

N R Konar *et al.* reported a case of naphthalene poisoning, presenting some unusual features. On admission to hospital the patient was semi-conscious, he looked pale and was deeply jaundiced. The pulse rate was 120, the temperature 99 F., and the respiratory rate 28. Twelve hours later the coma deepened, pallor became more marked, the heart sounds became feeble, and the temperature rose to 102 F. After a further 12 hours the condition became worse, the temperature rising to 103 F., the pulse rate to 142, and the respiratory rate to 44. There was evidence of right-sided hemiplegia. The patient died 3 days after swallowing the poison, the exact amount of which was not known. Examination of the blood showed haemoglobin 30 per cent, red blood-cells 2,410,000 per c mm and white blood cells 31,200 per c mm. The marked degree of anaemia was probably due to acute haemolysis, which increased the jaundice primarily caused by hepatic necrosis. The hyperthermia might be explained by the cholaemia resulting from liver necrosis, or by the formation in the body of an amino derivative of naphthalene-naphthylamine.

Konar, N R, Roy, H. K., and De, M N (1939) *Indian med Gaz*, **74**, 723

Leslie, A. (1939) *J. Amer med Ass*, **113**, 2229

Inorganic and Metallic

Mercury

Employed during cystoscopy—B H Page and C Wilson reported 3 cases of fatal mercurial poisoning after cystoscopy in which mercuric oxycyanide was employed. The occurrence of acute mercurial poisoning after cystoscopy might be due to one or more of the 3 following factors. The mistaken use of a highly concentrated solution, abnormal circumstances leading to excessive absorption of mercurial salt, or idiosyncrasy of the patient. In all of the cases reported the mercurial solution was left in the bladder after cystoscopy, and was not voided for some considerable time. In view of the rarity of the condition, the authors suggested that idiosyncrasy to the drug, possibly combined with abnormal retention and absorption of the solution, might have caused the fatalities. There is no doubt that the use of mercuric oxycyanide solution in cystoscopy is dangerous.

Sodium formaldehyde sulphonylate therapy—L A Monte and F Hull reported the results obtained from the use of sodium formaldehyde sulphonylate as an antidote to mercuric chloride poisoning. Treatment consisted of gastric lavage with a 5 per cent solution of sodium formaldehyde sulphonylate, 200 c cm of which were left in the stomach. An intravenous infusion, consisting of 10 g of sulphonylate dissolved in 200 c cm of water, was also given, and this was repeated in severe cases. The patients also received the usual measures employed in mercurial poisoning, such as parenteral administration of water, dextrose, and salt, intravenous administration of sodium bicarbonate, and blood transfusions. In a group of 40 patients thus treated, 14 (35 per cent) died, in 18 (45 per cent) toxic symptoms developed, and of these 18, 14 (78 per cent) died. In a group of 278 cases of mercuric chloride ingestion, previously reported by the authors, and in which no sulphonylate had been given, the mortality for the whole series had been 24 per cent, and for the patients who had developed acute mercurial poisoning, 53 per cent. The general results of sulphonylate treatment therefore appeared to be no better than those from other methods.

Iodine

W. H. Barker and W B. Wood reported 7 cases of severe febrile iodism in a series of 400 cases with hyperthyroidism treated with iodine, i.e. an incidence of 1.75 per cent. Common manifestations noted were fever, cutaneous eruptions, coryza, pharyngitis, enlargement of the lymph nodes, and eosinophilia. In one case jaundice developed. The pathological changes in the single fatal case consisted essentially of mild inflammatory perivascular lesions, which were present in most of the tissues. The continuation of iodine after marked symptoms of idiosyncrasy have developed may be extremely dangerous. Subsequent administration of iodine to patients in

whom iodism has developed in the past may or may not give rise to a second febrile reaction

- Barker, W. H., and Wood, W. B. (1940) *J. Amer. med. Ass.*, **114**, 1029.
 Monte, I. A., and Hull, L. (1940) *J. Amer. med. Ass.*, **114**, 1433.
 Page, B. H., and Wilson, C. (1940) *Lancet*, **1**, 640

Potassium Chlorate

W. J. Cochrane and R. P. Smith described a fatal case of accidental poisoning with potassium chlorate and reviewed the literature on the subject. In the case reported 30 to 35 g. (450 to 525 grains) of potassium chlorate was given in mistake for potassium chloride to a patient with nephritis and oedema. Death occurred within 9 days of the initial dose or 5 days after the last dose. Four days after the initial dose he complained of some pain in the neck and legs. Next day he commenced to vomit and had some diarrhoea. On the following day he complained of extreme weakness and pain across the upper abdomen. He had a dusky cyanosed appearance and exhibited an-hunger. His breathing was rapid, his pulse rapid and thready, and there was conjunctival icterus. The urine was scanty, smoky and dark brown in colour, and contained blood. The blood serum also was dark brown. There was marked tenderness in both lumbar regions. Coma was progressive. On post-mortem examination the muscles were found to be of a dusky colour. The lungs had a spongy consistence and were of a greyish-pink colour. Towards the bases posteriorly they showed oedema and congestion. The muscles and walls of the heart and aorta had a dusky grey appearance due to methaemoglobinaemia. The blood was dark brownish-red in colour and contained methaemoglobin. Examination of the stomach revealed an acute gastritis, and the intestines were collapsed and very pale, and showed a mild enteritis. The liver, spleen and kidneys were enlarged and filled with decomposition products of haemoglobin, the tubules of the kidneys were filled with brownish masses of blood detritus, giving a peculiar reddish-brown striping of the pyramids, which is said to be characteristic of potassium chlorate poisoning. The urine had a cloudy brown colour, and contained much albumin and a considerable amount of chlorate. From a review of the previously reported cases it appeared that, though considered rare, 161 cases (120 fatal) had been published. Witthaus having collected 155 examples up to 1911 (15 suicidal, 3 homicidal, and the others accidental). The fatal dose varied considerably, the smallest single dose being 14 g. (210 grains) in an adult. Apparently a certain amount taken in divided doses for a few days causes more severe reaction than if the same quantity is taken in one dose (Webster). Death usually occurs about 4 days after the first dose. The morbid changes are gastro-enteritis, a dusky grey appearance of the whole body due to methaemoglobinaemia, enlargement of the liver, spleen, and kidneys with much decomposing haemoglobin, and the brain is brown as if injected with chocolate. Haemolysis and transformation into methaemoglobin lead to asphyxia and the other symptoms, which begin 2 or 3 hours after the ingestion of the drug, with abdominal pain, vomiting, diarrhoea, followed by dyspnoea, cyanosis, low blood-pressure, cardiac failure, headache, giddiness, muscular weakness, restlessness, and coma. Treatment in acute cases the stomach should be washed out and intravenous injection of sodium bicarbonate given, and blood transfusion and inhalation of oxygen may be tried.

- Cochrane, W. J., and Smith, R. P. (1940) *Canad. med. Ass. J.*, **42**, 23.
 Webster, R. W. (1930) *Legal Medicine and Toxicology*, Philadelphia, p. 410.
 Witthaus, R. A. (1911) *Medical Jurisprudence, Forensic Medicine and Toxicology*, **4**, 690.

Alkaloids

Atropine Group

W. Muller records 3 cases of atropine poisoning after minimal doses. In one case 0.5 mg. was dropped into the conjunctival sac; in another 0.25 mg. was applied in an eye ointment, and in the third 0.7 mg. was taken by mouth in tablets. Vertigo and signs of collapse occurred and, though the effect was transient, the author recorded the cases to show the marked individual variations in sensitivity towards the alkaloid.

Nicotine

F. W. Adams refers to tobacco as now by far the most universally used narcotic. The reports of H.M. Customs and Excise show year by year an increasing consumption of and revenue from tobacco. During the year ended March 31, 1939, the yield from tobacco reached a new record and exceeded its nearest rival, beer, by more than £19,000,000, and figures from other countries tell much the same tale. The nicotineization of mankind is therefore advanced, but does this mean that by far the larger part of civilized mankind must be regarded as subject to a minor form of drug addiction? Two criteria to determine whether or not a substance is a drug of addiction are mentioned—one of the most striking properties of a drug of addiction is that its withdrawal causes very severe symptoms, 'the abstinence syndrome'. In the ordinary moderate smoker, though there may be some irritability, withdrawal does not produce these severe symptoms. Another feature of a true addiction drug is the tendency to cause relapse when an apparent cure has been obtained. In the ordinary moderate smoker, after abstinence for a certain time all craving vanishes. It is true that smoking is often resumed, this is generally due not to irresistible craving, but to allay that uncomfortable feeling of saintliness that assails one who does not smoke or drink when in company with those who do. There are, however, exceptions, such as the individual who smokes in bed, burns holes in the counterpane, and risks a general holocaust, and the continual chain smoker, these suffer severely in withdrawal and relapse again and again. The conclusion of the whole matter is that tobacco is a potential drug of addiction, which in particular cases becomes an actual one.

Peripheral vasospasm resulting from tobacco smoking—C. A. Moyer and W. G. Maddock discuss the peripheral vasospasm from the use of tobacco. Of all the substances produced by smoking tobacco, only nicotine and carbon monoxide are readily absorbed by the body. The average concentration of carbon monoxide in the blood of smokers is 0.52 volumes per cent. This quantity is too small to produce any physiological effect except at high altitudes. Nicotine undergoes more complete combustion in cigarettes and therefore more absorption takes place from pipes and cigars. The vasomotor reactions are due to the stimulating action of nicotine on the cells of the central and sympathetic nervous systems; this causes vaso-constriction and has some bearing on the aetiology of thrombo-angitis obliterans. Investigations were carried out on 20 normal subjects, after smoking the skin-temperature dropped and the blood-pressure and pulse-rate rose. Return to normal occurred in from 5 to 70 minutes and the temperature of the fingers always recovered before that of the toes. That these changes were not due to increased respiration during smoking was shown by smoking an empty pipe or tube, when they did not occur. Smoking through a water or ferric chloride filter produced the same changes in a lesser degree. In 2 patients with thrombo-angitis obliterans similar changes were recorded. In normal persons nicotine given by mouth did not produce the same results, but intravenously it did. Moyer and Maddock conclude that all tobacco must be avoided in the treatment of thrombo-angitis obliterans. It may also play some part in the aetiology of gangrene and other vasomotor disturbances such as endarteritis.

Adams, F. W. (1940) *Brit. J. Inebri.*, **37**, 172.

Moyer, C. A., and Maddock, W. G. (1940) *Arch. Surg., Chicago*, **40**, 277.

Muller, W. (1939) *Med. Welt*, **13**, 1230.

Cyclic Ureides and Barbituric Acid

Effect of Barbiturates on Gastric Secretion

R. J. Coffey *et al.* found that hypnotic and anaesthetic doses of barbiturates reduce both gastric and pancreatic secretions, and that the larger the dosage the greater is the reduction. The return to a normal flow is fairly prompt after hypnotic doses, but much more delayed following anaesthetic ones, such delay extending for as long as 4 days. Examination showed that the percentage of barbitone excreted in the gastric juice could rise as high as 5, but the amount excreted in the pancreatic juice was very small. The authors considered that gastric lavage in barbiturate poisoning is of little value unless constantly treated.

Treatment

Leptazol (cardiazol).—A. Heinrich reported on 42 cases of barbiturate poisoning which were all treated by the intravenous administration of large amounts of leptazol (cardiazol). The smallest dose employed was 5 c.cm. of a 10 per cent solution, and the patients were tested as to their somnolence by pinching and by attempts to wake them; if there was no response, the dose was increased by 5 c.cm. until results were obtained. Only in a few cases did epileptiform attacks supervene, and these were transitory, they indicated the upper level of cardiazol administration. It is important to remember that gas poisoning and morphinism are contraindications, as the author has repeatedly seen prolonged spasms, both clonic and tonic after administration of cardiazol in gas or morphine poisoning.

S. Kellner and T. Rudberg treated a case of barbiturate poisoning by intravenous injections of leptazol (cardiazol). The dosage employed was, on the first day, 62 c.cm., on the second, 105 c.cm.; on the third, 30 c.cm., and on the fourth, 40 c.cm. were injected. The corneal reflex appeared on the third day. Dextrose was added to the injections on the fourth day. The patient recovered, and, in the author's opinion, only the massive intravenous injections of the drug which constantly stimulated the respiratory centre enabled her to survive the first few days.

Picrotoxin. J. L. Lovibond and G. C. Steel reported a case of barbiturate poisoning which was successfully treated with picrotoxin. The diagnosis was confirmed by examination of the cerebrospinal fluid, when the cobalt nitrate and Millon's tests were found to be positive. She was treated with gastric lavage, lumbar puncture, intravenous saline, and intranasal oxygen but her condition did not improve. She was then given intravenous picrotoxin in divided doses of 2.0 c.cm. of a 0.3 per cent solution. In less than 3 hours she was sufficiently recovered to hold and drink from a tumblerful of water. She was given a total of 54 mg. of picrotoxin and also 112 c.cm. of coramine. The coramine was given after the picrotoxin had begun to take effect to maintain its good results. Lovibond and Steel consider such a large dose of picrotoxin to be quite safe in a case of severe poisoning.

F. C. Reifenshein, Jr., and L. C. Reifenshein reported 2 cases of poisoning with barbituric acid compounds, one that of a woman who had swallowed 245 g., and the other a man seen 10 hours after he had consumed 15 g. They suggested that the following technique should be employed: (i) gastric lavage, and the use of sodium phosphate as a purgative, (ii) continuous oxygen in a tent, (iii) 50 per cent sucrose solution intravenously to produce diuresis, alternating with 5 per cent intravenous dextrose to supply fluids, (iv) with either of these solutions, picrotoxin is given, in the first case reported above 314 mg. were administered in 3 days. Further measures may include a catheter tied in the urethra, lumbar puncture to relieve intracranial pressure, and, if necessary, transfusion should anaemia develop.

G. M. Slot employed picrotoxin in a case of barbiturate (soneryl) poisoning in a woman aged 26 years, who had taken possibly 65 grains of soneryl. She became comatose and cyanosed with a low blood-pressure and a feeble pulse. The stomach was washed out and filled with strong black coffee and 1 fl. oz. of castor oil. Intravenous glucose-saline and heart stimulants were also given. In spite of this treatment the patient's condition deteriorated. Lumbar punctures were performed, but she did not recover. 1.5 c.cm. of an 0.3 per cent solution of picrotoxin were then given every 20 minutes intravenously. After 4 doses the drug was given intramuscularly throughout the night, another 2 c.cm. being given intravenously in the morning. The patient gradually recovered from the beginning of this treatment, having been in coma between 60 and 70 hours.

S. W. Gillman reported 5 cases showing the use of picrotoxin in the treatment of collapse due to barbiturates. Prolonged deep narcosis is useful in the treatment of acute mental disturbances. Barbiturates, often used in this respect, are removed either by oxidation or through the kidneys. If the oxidation is slow, and the narcosis therefore correspondingly deep and prolonged, dangerous collapse may occur. Picrotoxin neutralizes this condition by increasing the respiration and the oxygen consumption. In 4 of the 5 cases reported medinal-luminal (barbitone-sodium-phenobarbitone) narcosis had been induced. In the fifth the patient had attempted suicide by taking 100 gr. of medinal. A 1 in 1,000 solution of picrotoxin was given

in intravenous doses of 10 c.cm. hourly until the patient had recovered. There was one death, from heart failure, in this series.

Coffey, R. J., Koppanyi, T., and Linegar, C. R. (1940) *Amer. J. digest Dis.*, **7**, 14.

Gillman, S. W. (1940) *Lancet*, **1**, 598.

Heinrich, A. (1939) *Klin. Wschr.*, **18**, 1410.

Kellner, S., and Rudberg, T. (1939) *Nord. Medicin*, **4**, 3006.

Lovibond, J. I., and Steel, G. C. (1939) *Lancet*, **2**, 561.

Reifenstein, E. C., Jr., and Reifenstein, E. C., Sen. (1939) *Ann. intern. Med.*, **13**, 1013.

Slot, G. M. (1940) *Brit. med. J.*, **1**, 849.

Abortifacients

Oxytocic drugs

Quinine—C. K. Vartan and G. Discombe reported a case of death from quinine poisoning in a woman of 34. The clinical picture was almost indistinguishable from the most severe form of blackwater fever though the woman had never been out of England and had never had malaria. She appeared to have taken a total of 6.08 g. of quinine sulphate or 5.04 g. (77.7 grains) of the pure alkaloid as an abortifacient. She developed headache, vomiting, pyrexia, abdominal pain and increased pulse rate. The body became covered with a copper-coloured rash which did not fade on pressure. Urine drawn by means of a catheter was black. Examination of the latter showed nothing but masses of amorphous yellow deposit and a slightly excessive number of white blood-cells. It was sterile and contained methaemoglobin in a very high concentration. Examination of the blood showed severe anaemia and very dark serum due to the presence of methaemoglobin. The patient died in a drowsy state on the tenth day. At necropsy there was some degeneration of the kidney and liver; most of the renal tubules were choked by a granular amorphous yellow deposit, but there was no nephritis.

Vartan, C. K., and Discombe, G. (1940) *Brit. med. J.*, **1**, 525.

Chromium Poisoning

J. F. Sander and C. D. Camp reported a rare case of chromium poisoning in a female infant aged 14 months. The child was known to have eaten some paint containing an insoluble chromium compound. Stupor developed followed by convulsions and the pupils were dilated. The convulsions resembled Jacksonian epilepsy and the temperature was 103° F. The gastro-intestinal tract was unaffected, but the throat appeared to be inflamed. The cerebrospinal fluid was normal and the neurological findings were negative. Chromium was isolated from the urine and faeces. The infant was treated with sedatives, intravenous Ringer's solution, 2 blood transfusions, magnesium sulphate enemas, and iodide of iron by mouth when possible. She made a slow, but steady, recovery with no paralysis, or impairment of her reflexes or special senses.

Sander, J. F., and Camp, C. D. (1939) *Amer. J. med. Sci.*, **198**, 551.

TOXICOLOGY INDUSTRIAL POISONING

See also B. E. M. P., Vol. XII, p. 127, Cumulative Supplement, Key Nos. 1528-1540, and Surveys and Abstracts 1939, p. 570.

Mercury

Mercury Fulminate

Since September, 1939, M. Joltrain *et al.* have observed patients with disorders due to their work in cartridge factories. These fell into 3 groups. (i) The most important and interesting were allergic and due to contact with dry fine fulminate, especially among those workers who had just entered the industry. The manifestations included paroxysmal haemoglobinuria, spasmodic coryza, angioneurotic (Quincke's) oedema, and eczema, particularly of the face and upper limbs. It is suggested that hepatic insufficiency, often alcoholic, may play a part in the aetiology of these cases, and that this should be borne in mind from a therapeutic point of

view. (ii) Cases, of which 2 are reported, of general intoxication by gases which have accidentally gained access to the workshop, namely toxic fumes of fulminate from waste material discharged from other parts of the factory. One of the two reported patients had an enlarged liver. The symptoms resemble those of poisoning by carbon monoxide and illuminating gas. (iii) The well-known dermatoses and microbial (staphylococcal and streptococcal) forms of inflammation of the skin, which may resemble burns, and may follow irritation of exposed parts of the skin by nitrous fumes and some soaps and oils.

Joltrain, M., Hissard, R., and Boulard, F. (1939) *Bull. Acad. méd. Paris*, **122**, 692

Manganese

Chronic intoxication by manganese may be confused with other affections of the central nervous system, as the main symptoms are those of an extrapyramidal cerebral affection. In the differential diagnosis, progressive lenticular degeneration must first be considered. In this condition cirrhosis of the liver, marked hypertonus, choreo-athetosis and, in later stages of the disease, contractures of the limbs are characteristic. In manganese intoxication, however, muscle tonus was diminished in a case observed by L. de Lisi, and was normal or slightly increased in the lower limbs. Hypertonus in the upper limbs, the attitude of body and head, and steppage gait are important signs in differentiating manganese intoxication from Parkinson's disease and encephalitis epidemica.

de Lisi, L. (1939) *Riv. Patol. nerv. ment.*, **54**, 349

Toxic Gases

Fluorine and its Compounds

Causing osteosclerosis—J. Wilkie records 2 cases of osteosclerosis in 2 male workers in a Sheffield factory, aged 47 and 64, who had been employed there for 3½ and 16 years respectively. The younger man, who was much the more severely affected, was engaged in the preparation of aluminium fluoride; he had had attacks of hæmoptysis not proved to be tuberculous, weakness for 6 months, and rheumatic pains in the legs, back, and lower chest, the chest pain being brought on by exertion, and stopping when work was discontinued. The older and healthy man, who was engaged in the preparation of hydrofluoric acid, was examined because he worked in the same factory as the younger man. In review of the subject attention is directed to the occurrence of mottled teeth in children and young adults in places where the drinking water contains appreciable quantities of fluorine compounds, and in breast-fed infants whose mothers are working in factories where they handle cryolite (a double fluoride of sodium and aluminium). F. P. Møller and V. Gudjonsson in 1932 first described the skeletal lesions, which they found in 30 out of 78 cases examined for pulmonary changes. The following lesions were found in some of the 78 cases: silicosis in about half the total, presumably due to quartz, a contaminant of cryolite, acute gastric symptoms—nausea, vomiting and loss of appetite—in more than half the cases, anaemia with a low red-cell count and a high colour index, ascribed to destruction of the bone marrow. Wilkie could not find any record of fluorine osteosclerosis among industrial workers in Great Britain, and points out that his 2 cases were not exposed to silica. All the bones may be affected with diffuse osteosclerosis, new bone being formed by periosteum and endosteum, the medullary cavity is diminished, and calcification occurs in ligaments which are not so affected except in old age.

Møller, F. P., and Gudjonsson, V. (1932) *Acta radiol., Stockh.*, **13**, 269

Wilkie, J. (1940) *Brit. J. Radiol. N.S.*, **13**, 213

Benzene (Benzol)

P. A. Davis discussed the toxic symptoms resulting from the industrial use of benzene (benzol, C_6H_6) and their prevention. The substance is used in such processes as colour printing and clothes cleaning. It may enter the body by the respiratory system, the alimentary system, or the skin. The first of these is the most common way. The last two only occur when the concentration of the fumes is very great.

Men become immune to minute amounts taken over a period of months, but once this amount is increased, symptoms begin to appear. Many toxic symptoms may be produced, varying from slight giddiness and excessive fatigue to laboured respirations and coma. The blood picture shows characteristic changes. There is first a slight leucocytosis, then leucopenia, then anaemia which gradually becomes worse as the absorption increases. Determination of the urine sulphates is one of the best methods of ascertaining the extent of the poisonous action. The estimation should be made frequently in benzene workers. Proper ventilation, the employment of only healthy workers, the substitution of less poisonous solvents for the benzene, and the proper education of the supervisors and workers are all methods of preventing the poisonous reactions.

Morbid Anatomy

T. B. Mallory *et al.* discussed the pathological results of chronic exposure to benzene. They examined 19 cases, 14 autopsies and 5 biopsies, and reported their history, clinical examination, and pathological findings in detail. In the bone marrow they found various changes. Hyperplasia or hypoplasia may occur. The former occurred only after long exposure to benzene and the latter was commoner in females, though it occurred after any length of exposure. Changes were also found in the entire haemopoietic system. Two patients suffered from leukaemia. Both these patients were males, and other observers have found leukaemia from chronic benzene poisoning commoner in this sex. In one case the cells showed mitotic figures similar to those found in some malignant tumours. Hyperplasia of the marrow in the presence of anaemia was commoner than hypoplasia in this series, and the appearances were similar to those which have been described in chronic radium poisoning.

F. T. Hunter dealt with the clinical effects of chronic exposure to benzene in 89 patients and gave detailed reports of some of them. He found that susceptibility was the same in both sexes. No immunity is acquired by exposure to the fumes and even the smallest traces may lead to poisoning if the exposure is long enough. Clinical signs of poisoning may appear long after exposure with the onset of an infection. The benzene attacks the haemopoietic system and may give rise to leucocytosis, leucopenia, leukaemia, anaemia, polycythaemia, eosinophilia, or immature cells in an otherwise normal blood. The spleen may be enlarged. In this series 10 of the cases proved fatal, all these patients being anaemic, in one there was a decrease in the absolute number of polynuclear leucocytes, and in 2 cases a relative eosinophilia.

Industrial Aspects

The industrial aspects of chronic exposure to benzene were discussed by M. Bowditch and H. B. Elkins. They estimated the benzene vapour concentration in various workrooms such as artificial leather plants and rooms in which crepe rubber soles were cemented to shoes with a benzene compound. They described the methods of estimating these two factors and discussed the relative usefulness of the two estimations. They concluded that, if properly carried out, both factors gave valuable information. They found the vapour concentration in the workrooms varied and in one case was as high as 420 p.p.m. The concentration naturally varied with the type and efficiency of the ventilation. When natural ventilation was used the concentration was affected by the weather, a lower benzene exposure being found in the winter. It has been shown that the ratio of inorganic sulphates to total sulphates in the urine is lowered if there is an absorption of benzene. The samples taken from benzene workers were unaffected by the day of the week on which they were taken, but the ratio was markedly lower in the afternoon than in the morning. In 8 fatal cases of benzene poisoning the concentrations of the vapour were from 100 to 200 p.p.m., 100 p.p.m. is considered the safest height to which the concentration may be allowed to rise, but the authors have seen cases of poisoning in which it was below 75 p.p.m. The limit of safety for the urine sulphate ratio is 50 per cent, and this value cannot be correlated with any vapour concentration.

Blood Picture

L. A. Liff and C. P. Rhoads discussed the haematological effects of benzene poisoning. They investigated the sternal bone marrow in 9 cases by biopsy, also

the condition of the blood, the liver function tests, the renal function tests, and the excretion of urobilinogen. Eight of these cases recovered and 1 died of leukaemia. The haematological findings varied. Anaemia, leucopenia, and thrombocytopenia were found. All cases showed a raised reticulocyte count. Increased fragility of the cells was present in one case. Sternal biopsy showed hyperplasia in some cases and hypoplasia in others. All the patients had free acid in the gastric juice and there was no X-ray evidence of gastro-intestinal abnormality. Serum urobilin was raised in 5 of 6 patients, but it was normal in 1 who had very little anaemia. The icterus index was raised in 4 of 5 patients. The urobilinogen level in the faeces was raised in 8 of 9 patients. After suitable treatment with liver, etc., for 2 to 5 months, 8 of the 9 patients were clinically improved. The variable blood findings were thought to be due to the different concentrations of the fumes and the length of exposure, and to individual susceptibility. Animal experiments have shown that this susceptibility may depend on a dietary factor.

M. Lamy *et al.* reported on 10 cases of chronic benzene poisoning among shoe workers, 5 of these were fatal. Although exposure to benzene had been prolonged by as much as 17 years, the symptoms of poisoning occurred quite suddenly when a new substance containing 80 per cent. was introduced into their occupation. The clinical picture of poisoning comprised anaemia, a fall in the red-cell count, haemorrhages, decrease in the number of blood platelets and white cells, especially granulocytes, increase in the bleeding time, with fever in some cases. In the fatal cases, post-mortem examination revealed changes both in the bone-marrow and the liver. In 3 of the fatal cases there was almost complete aplasia of the bone marrow. Treatment, consisting of blood transfusion, gave good results.

I. Gray *et al.* reported a case of benzene (benzol, C_6H_6) poisoning from the inhalation of benzene fumes during work. The case was of interest for the following reasons. The white-cell blood-count was 2,800 on admission, but, in spite of a direct transfusion of 300 c.c. of whole blood given within a few hours, it fell to 1,600 within 24 hours, and to 500 within 48 hours. It never rose above 900 during the remaining 12 days of the patient's life. Urinary sulphate studies showed that 95 per cent. of the total sulphates were excreted as inorganic sulphates. In performing the grouping and cross-matching preliminary to a fourth transfusion, the patient's cells were agglutinated by both testing sera, although on three previous occasions the patient had been found to belong to Group O. Moreover, the patient's serum agglutinated the cells of a potential donor of Group O. On further study this difficulty was found to be due to the presence of an auto-agglutinin.

Bowditch, M., and Elkins, H. B. (1939) *J. industr. Hyg.*, **21**, 321.

Davis, P. A. (1940) *J. Amer. med. Ass.*, **114**, 553.

Erf, L. A., and Rhoads, C. P. (1939) *J. industr. Hyg.*, **21**, 421.

Gray, I., Greenfield, I., and Lederer, M. (1940) *J. Amer. med. Ass.*, **114**, 1325.

Hunter, F. T. (1939) *J. industr. Hyg.*, **21**, 331.

Lamy, M., Kissel, P., and Pierquin, L. (1939) *Sang.*, **13**, 467.

Malloy, T. B., Gall, I. A., and Brickley, W. J. (1939) *J. industr. Hyg.*, **21**, 355.

Nitro- and Amino-Derivatives

Porphyrinuria in Chemical Workers

According to C. Rimington and M. W. Goldblatt acute symptoms from the inhalation of aromatic nitro- and amino-derivatives are now rare in industrial workers. In an investigation into the chronic results of the long-continued absorption of small amounts of these bodies, the urinary excretion was found to be considerably increased in the workers but none of them were cyanosed or had any signs of toxicity. It is suggested that investigations should be undertaken into the incidence of those sensitive to poisoning by these substances in order to decide when an affected person may safely return to work.

Rimington, C., and Goldblatt, M. W. (1940) *Lancet*, **1**, 73.

Vanadium

Dr Symanski examined the workers in a large factory where vanadium and its

compounds were used to a great extent. Vanadic acid is an irritant of the mucous membrane, but not very toxic after absorption. The symptoms of vanadium pentoxide poisoning are very characteristic; conjunctivitis, rhinitis, aqueous coryza, chronic bronchitis (but without any signs of inflammation of the parenchyma of the lungs). It is possible for bronchiectases and specific pulmonary infection to develop upon the basic bronchitis after some time.

The author did not find any gastro-intestinal symptoms as described in the literature. There were also no renal, nervous, ocular or anaemic symptoms.

von Symanski (1939) *Klin. Wschr.*, **18**, 1455.

Radium Poisoning

Measures have been taken to provide deep burial of radium so as to obviate the serious risks which would result from liberation of radium stored in hospitals and other institutions by bombing. J. Read of the Mount Vernon Hospital and Radium Institute, Northwood, Middlesex, reviews radium poisoning in relation to war risks, and points out that if radium were to be dispersed by a bomb it would be very difficult even with the most sensitive radium detector available to be certain that there was not any potentially lethal pocket left unburied, and that with its half-life of 1,600 years it would retain its powers for centuries. This review deals mainly with radium poisoning as seen in luminous watch dial workers, drinkers of radium water nostrums, patients receiving intravenous injections of radium salts, and the risks of inhalation of dust in mines, as those in the Scheeburg district and in the pitch-blende mines of Joachimstal, where, probably for centuries, there has been a high mortality from primary carcinoma of the lung among the miners. Most of the information about the distribution of radium in the body has been derived from observations made after intravenous injection or ingestion of soluble radium salts; according to Martland even when soluble bromides or chlorides are absorbed they are precipitated in the blood stream as insoluble sulphates of colloidal or particulate size in the reticulo-endothelial cells, especially in the bones, liver, and spleen; the skeleton suffers most and the radium is excreted from the bones very slowly. The symptoms—anaemia of the aplastic form, absorption of bone and fibrous replacement which can be shown radiologically—do not usually appear for a considerable time, though a man injected with 1 mg. of radium in September died in the following December. Radium sulphate dust inhaled is probably much more dangerous than when ingested as it would remain there, a fraction of a microgram of radium has produced primary carcinoma of the lung (Rajewsky).

Martland, J. (1929) *J. Amer. med. Ass.*, **92**, 466.

Rajewsky, B. (1936) *Strahlentherapie*, **56**, 703.

Read, J. (1939) *Brit. J. Radial.*, N.S. **12**, 632.

TRACHEA DISEASES

See also B.E.M.P., Vol. XII, p. 200; Surveys and Abstracts 1939, p. 573.

Obstruction

Tumours

Sarcoma—T. Weinberg of the Mount Sinai Hospital, New York, records 2 cases and collects 6 more since 1929 when R. D'Aunoy and A. Zoeller found, among 261 primary tumours of the trachea, 26 authentic primary sarcomas, thus bringing the total up to 34. These rare tumours are of slow growth and low malignancy, and usually occur in the earlier decades of life; they arise from the upper part of the trachea, its lateral or posterior surface, by a broad base, but sometimes are polypoid. Microscopically the growths are commonly spindle-celled but may be round-celled. In one of Weinberg's cases the appearances were those of a myxosarcoma in possibly a mixed tumour of the salivary gland type.

D'Aunoy, R., and Zoeller, A. (1929) *Arch. Path.*, **2**, 589.

Weinberg, T. (1939) *Amer. J. Cancer*, **37**, 201.

TRACHOMA

See also B.F.M.P., Vol. XII, p. 209; Cumulative Supplement, Key No. 1545; and Surveys and Abstracts 1939, p. 573.

Epidemiology

Aetiology

L. Poleff stated that the inclusion bodies form the aetiological factor in trachoma. He published photomicrographs showing various stages of evolution *in vitro* (see Plates III and IV). He considered the Rickettsia-like corpuscles, stated by Busacca to be the cause of trachoma to be identical with the inclusion bodies when they are not cellular or other debris.

A. Cuénod and R. Nataf disagree with Foley and Parrot in their conception of the so-called 'plastilles' (granules) of trachoma and of their specificity for trachoma. The authors state that the typical punctate granules occur only in trachoma. The presence of these granules or of protoplasmic debris with the specific punctations decides the diagnosis. The punctations or corpuscles in the 'plastilles', and those in the epitheloid cells of the trachoma follicles, are either micro-organisms embedded in protoplasm or a special reaction of the cytoplasm to the trachoma virus. The authors think, although it cannot be proved yet, that the punctations are analogous to Prowazek corpuscles, or rickettsias. There are some similarities between rickettsias and the virus of trachoma: polymorphism, affinity for certain dyes, impossibility of cultivation in inert media, and possibility of cultivation in certain organs, such as the intestine of the louse.

The authors propose, in agreement with Burnet (Director of the Pasteur Institute in Tunis), to name the corpuscular virus of trachoma *Prowazekia trachomatis* in view of the position not being quite clear yet and in honour of the works of Prowazek.

Cuénod, R., and Nataf, R. (1939) *Arch. Ophthal.*, Paris, **3**, 592.

Foley, H., and Parrot, L. (1939) *Arch. Ophthal.*, Paris, **3**, 230.

Poleff, I. (1939) *Brit. J. Ophthal.*, **23**, 738.

Treatment

Sulphapyridine

A. F. MacCallan reports on the use of sulphapyridine in trachoma. The dosage for adults was 3 g. on the first day, divided into 6 doses, with an equal quantity of sodium bicarbonate, then a daily amount of 2 g. was given in the same way for 9 days. In one case bacteriological cultures before treatment showed a heavy growth of pneumococci and haemolytic streptococci, after treatment with sulphapyridine there were only a few sparse colonies of non-pathogenic staphylococci and diphtheroids. There had been some blepharitis which was cured by treatment, but the phenomena of trachoma remained unaltered. In the author's opinion the good results reported in the treatment of trachoma by sulphonamide drugs have been obtained by the elimination of superimposed bacterial infections. The sulphonamides have not proved effective in virus diseases, but they are expected to be of value in bacterial conjunctivitis and blepharitis.

Sulphanilamide Therapy

L. A. Julianelle *et al.* investigated the effect of sulphanilamide in trachoma. The dosage employed was $\frac{1}{2}$ grain per pound of body weight, by mouth, for the first 10 days, then $\frac{1}{4}$ grain per pound for the next 14 days. Recovery occurred in 20 per cent of the cases, varying degrees of improvement in 40 per cent, and no improvement in the remainder. The drug had a marked and rapid effect on the secondary infections commonly associated with trachoma. The most striking results were observed in patients with exacerbative disease. In 6 patients studied, epithelial cell inclusions disappeared during treatment.

R. D. Harley *et al.* reported the results of treating 11 cases of trachoma with sulphonamides. In all cases treatment was successful, but cases of the disease in stages II and III (MacCallan's classification) showed the best results. Four of the patients showed toxic reactions of sufficient severity to call for cessation of the drug, but treatment was successfully carried on with neoprontosil. The latter proved far less toxic. Trachoma probably requires only low or moderately low concentrations of sulphanilamide in the blood (3 mg. per 100 c.cm.). A usual daily dose of sulphanilamide was 60 grains and of neoprontosil 45 grains. The period of treatment varied from 8 to 62 days. Neoprontosil is probably more suitable for the treatment of trachoma when the drug must be given over a long period. Sulphanilamide, however, gives the more striking results.



Photomicrographs demonstrating what L. Poleff believes to be the aetiological agent of trachoma in several stages of development. The material for A-D was obtained by cultivation for 10 days in tissue cultures of a trachomatous conjunctiva which showed very few elementary bodies and no inclusion bodies. A. Classical appearance of epithelial cell crammed with elementary bodies. B. Voluminous inclusions consisting of initial bodies in process of division. C. Ruptured epithelial cell full of mulberry-like inclusions. D. Free initial and elementary bodies. E. Elementary bodies in an epithelial cell from a trachomatous conjunctiva for comparison. A. D. 1,000. E. 2,000.

(This and Plate IV from *British Journal of Ophthalmology* 1939)

PLATE III



D



F

For legend see Plate III.

PLATE IV

F. Jasseron and G. Morard employed sulphonamide compounds in almost 200 cases of trachoma. They found that symptoms such as pain, photophobia, and laceration disappear in 48 hours. Pannus and infiltration of the cornea are absorbed in 8 days. Corneal ulcers heal in 36 hours. Healing is greatly accelerated, and, in 75 per cent of cases, cure is obtained in 3 weeks. Superadded infections, with the Koch-Weeks bacillus, the Morax-Axenfeld bacillus, the pneumococcus, and the gonococcus are cured in 4 days. The dosage varies according to the age of the patient: 1 or adults, 2 g. daily is given for 5 days, 1.5 g. for 4 days, and 1 g. for 4 days. For children between the ages of 8 and 12, the dosage is 1.5 g. daily for 4 days, 1 g. for 4 days, and 0.5 g. for 4 days. For children between the ages of 4 and 8, 1 g. is given daily for 4 days, 0.5 g. for 4 days, and 0.25 g. for 4 days. In most cases a modified local treatment is adopted; silver nitrate, 1 in 100, is applied to the lids for the first 4 or 5 days; atropine, 1 in 100, is employed when there is ciliary infection, or contraction of the iris, and an occlusive dressing is employed when there is corneal ulceration.

Treatment of Sequelae

Trachomatous recurrent ulcerative keratitis.—A. Bray reports the use of neoprontosil (prontosil soluble) by instillation in the treatment of recurrent trachomatous ulcerations of the cornea. The case reported had had severe pain in the eyes for several years and had been treated for two years without obtaining relief. On examination a diagnosis was made of trachomatous recurrent ulcerative keratitis superimposed upon trachomatous pannus. Vision in the right eye was reduced to very poor light projection, the left eye also showed pannus formation at the corneal periphery, and vision was 6/60. Under cyan anaesthesia the upper tarsal plates of both eyes were removed and grattage was performed on both lower lids. The left eye made a rapid recovery but the right eye remained troublesome and recurrent ulcerations of the cornea requiring cauterization appeared weekly. Carbolic acid and trichloroacetic acid were used as cauterizing agents and 'every drug known for instillation', nothing apparently could stop the recurrent ulcerations. As a last resort one drop of a 2.5 per cent solution of neoprontosil was instilled into the eye 3 times a day, the patient could not tolerate suphanilamide internally and this was discontinued after 3 doses. Five days after the commencement of the neoprontosil instillations the patient was free from pain, no further ulceration appeared, the photophobia disappeared in 3 weeks, the conjunctival redness began to disappear, the cornea cleared, and the vessels showed signs of disappearance, in one month the patient began to walk about without dark glasses and was perfectly comfortable and happy. The author believes this is the first case reported in which neoprontosil has been used by local instillation. Without drawing conclusions from one case the author suggests that it should be given a trial in all recurrent ulcerations of the cornea and in all protracted infective ulcerations of the cornea.

Bray, A. (1939) *Amer. J. Ophthalm.*, **22**, 901.

Harley, R. D., Brown, A. L., and Herrell, W. I. (1939) *Proc. Mayo Clin.*, **14**, 641.

Jasseron, F., and Morard, G. (1940) *Pr. méd.*, **48**, 234.

Juhanelle, J. A., Lane, J. T., and Whitted, W. P. (1939) *Amer. J. Ophthalm.*, **22**, 1244.

MacCallan, A. I. (1940) *Brit. med. J.*, **1**, 482.

TROPICAL ULCER

See also B. L. M. P., Vol. XII, p. 256.

Treatment

Sulphonamide Compounds

K. V. Earle described a series of cases of tropical ulcer treated with sulphonamide compounds. Local treatment of the usual types (copper sulphate, magnesium sulphate and glycerin to clean dirty ulcers; cod-liver oil, and scarlet red sulphionate to promote epithelialization) was continued at the same time. Sulphapyridine by

mouth, in a daily dosage of 3 g., was used in some cases, and sulphanilamide in others. It was found of very little value in long-standing ulcers. Only 2 cases out of 6 were cured. Recent ulcers of not more than 1 month's standing responded better. Fourteen cases out of 38 healed within 2 weeks. Twelve pre-ulcerative vesicular cases were prevented from ulcerating.

Farle, K. V. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 105.

TUBERCULOSIS

See also B I M P., Vol. XII, p. 286; Surveys and Abstracts 1939, pp. 39 and 577, and p. 94 of this volume.

Epidemiology

I. W. Flahiff presents evidence to show that persons who react to tuberculin are less likely to develop manifest tuberculosis when they are later exposed to a known source of infection than are those who do not react to tuberculin and then are similarly exposed. The observations were made at the Mental Hospital, Kingston, Jamaica, between June, 1932, and June, 1938, the patients being predominantly negro and almost entirely adult (average age, 35). Routine tuberculin tests on admission were made at intervals of 2 weeks and an X-ray picture was taken in the following week. The population of the institution is fairly constant at 2,000, annual deaths vary between 225 and 260, of which 50 to 60 are due to pulmonary tuberculosis. Patients were grouped according as they reacted to tuberculin, namely, those reacting to 0.01 mg., those reacting to 1.0 mg., and those with no reaction to tuberculin. Repeated X-ray examinations were made, those reacting on admission being examined at intervals of 8 months and those who did not react every 3 or 4 months. Classification of manifest tuberculosis was made chiefly on the basis of X-ray pictures. During the study 1,295 persons reacted to 0.01 mg. of O.T. on admission; 454 to 1.0 mg. of O.T., and 206 failed to react. In these groups, during the period of observation, 50 cases of tuberculosis developed among the 1,295, with 39 deaths, 42 among the 454, with 33 deaths, 39 among the 206 non-reactors, with 27 deaths. The diagnosis of tuberculosis was confirmed in the great majority of cases by necropsy and in the remainder by X-ray or clinical examination before death. The observations show that in this institution, in which tuberculosis was prevalent, the rate of onset and the death rate from the disease were higher in those who did not react to tuberculin on admission than in those who were sensitive to tuberculin when admitted. Persons with the less sensitive reaction (1.0 mg.) acquired tuberculosis in a higher percentage of instances than in those with a strong reaction (0.01 mg.).

Seasonal Variations in Lesions

C. Clayton discussed the seasonal variation in tuberculous lesions—this variation can be easily detected only in visible lesions, i.e. those of the skin and glands. He analysed the data concerning the appearance of axillary and cervical glandular enlargement and suppuration in these glands in 420 patients, and also the seasonal variation in the glands of an additional 43 patients who had relapsed after previous attacks. The maximum incidence of glandular swelling was in January, with a rapid diminution in the spring. The minimum number of cases occurred in August and September with a gradual rise in the autumn to a peak in December. In 262 patients the glands supplicated and this occurred most often in March and April, and was lowest from August to October.

Retardation of the Decline of Respiratory Tuberculosis in Young Adults

In a statistical study of tuberculosis and social conditions in England with special reference to young adults, P. D'Arcy Hart and G. Payling Wright have reinvestigated the retardation in young adults (15–24) of the general decline of respiratory tuberculosis. Comparatively soon after the publication of the early Annual Reports of the Registrar-General in the last century it became clear that the recorded mortality from respiratory and other forms of tuberculosis was falling in England and Wales. But since 1922 in London and 1928 elsewhere in this country it has been recognized that young adults, more particularly young women, no longer

take their share in the general reduction of the mortality from respiratory tuberculosis. In 1934-36, however, the mortality for young males showed a sudden improvement, but for young females, in whom the set-back was much more severe, the position was left serious. The authors consider that the retardation began in the country as a whole about 1901 to 1905 for young women, and about 1913 for young men. Several individual possible responsible factors for this retardation have been previously investigated, but the authors of this report decided that the retardation must depend on the interaction of several factors. The retardation has affected all parts of the country, but to different degrees, though on the whole the urban areas, especially London and the county boroughs, have been more seriously involved. No corresponding retardation in the decline in mortality from 'diseases other than phthisis' took place among young men and women. From evidence obtained from a study of the county boroughs, this difference is ascribed 'to a lesser sensitiveness of these young to social conditions as regards the very heterogeneous collection of diseases that this composite term embraces'. The evidence collected for this report is against the hypothesis that the retardation in the phthisis mortality decline among young adults has been due to diminished tuberculinization in childhood with resulting reduced immunity in adolescence. The suggestion is made that the retardation is due to (a) a predisposing factor, i.e. the special sensitiveness of young adults, in comparison with persons of other ages, to social conditions, as regards their mortality from respiratory tuberculosis, (b) general determining factors, i.e. the contemporaneous wide changes in social and economic trends, such as unsatisfactory housing conditions and increased industrial employment of young women, factors which were active at the beginning of this century, (c) local determining factors, especially housing conditions.

Clayson, C. (1939) *Brit. J. Tuberc.*, **33**, 152.

Flahiff, E. W. (1939) *Amer. J. Hyg.*, **30**, 69.

Hart, P. D'Arcy, and Wright, G. Payling (1939) *Tuberculosis and Social Conditions in England with Special Reference to Young Adults*, London: National Association for the Prevention of Tuberculosis.

Clinical Picture

Initial Articular Symptoms

Non-specific articular disorders are known to occur as manifestations of tuberculous toxæmia. J. Heimbeck reported a case of primary tuberculosis in which there appeared initial articular symptoms. This patient had been in good health until she suddenly developed pain in the knees, left elbow, and the right hip and finger joints. The ankles were swollen, but not painful. On examination nothing abnormal was found in the body or the urine, and there was no pyrexia. The von Pirquet test was negative. Six weeks later another tuberculin test gave a maximal positive reaction, but X-rays failed to show any tuberculous lesion. Ten weeks after the onset of the articular symptoms, X-rays showed a well-defined infiltration the size of a small pea in the second intercostal space. Two weeks later another radiograph revealed a right pleural effusion with no change in the infiltration. Another examination two months later showed a diminution of the effusion and incipient cicatrization. The author considered that specific primary toxins of tubercle bacilli may exist in the absence of a positive tuberculin reaction.

Heimbeck, J. (1939) *Acta paediatr., Stockh.*, **28**, 206.

Differential Diagnosis

Bacteriological

V. I. ester isolated 130 strains of acid-fast saprophytic bacilli from human material examined at the Danish State Serum Institute in 4 years. The number increased when the technique was improved by introduction of an egg-asparagin medium containing 0.75 per cent of glycerin instead of Petroff's medium, and by the replacement of sodium hydroxide by 6 per cent sulphuric acid for homogenization. For differential-diagnostic purposes prolonged observation of the primary culture, a subculture on solid egg medium and in Besredka's fluid medium, and intracutaneous injection into guinea-pigs are recommended. The saprophytic strains were not

pathogenic to guinea-pigs, but some were able to produce small abscesses after intracutaneous injection

Lester, V. (1939) *Acta tuberc scand.*, **13**, 251

Diagnostic Tests

Vollmer Patch Test

H. Vollmer reports on the tuberculin patch-test in 3 groups of children, totalling 2,000. Among 847 children in one group there was only one case with clinical, radiographic, or bacteriological evidence of tuberculous infection which did not give a positive reaction to the patch test, this was in a child with miliary tuberculosis, in whom the Mantoux test with 1.0 mg. of old tuberculin was also negative. Among another group of 540 children, 535 had active tuberculous lesions, and 529 of the latter gave a positive patch test, of the six cases who failed to react to the patch test, 4 were known to be negative anergic, and also to show negative reactions to the Mantoux test with high tuberculin concentrations. Only 2 cases were really missed by the patch test: one of these was a child with anergy who reacted only to the Mantoux test with second strength purified protein derivative. A mass examination of 613 high-school students was carried out with the Mantoux test, the patch test, and X-ray examination. No significant lesions were missed, if patients failed to react positively to either the patch or Mantoux tests. Among 2,000 children with 763 positive reactors to tuberculin, 3 cases with active tuberculosis were missed by the patch test, one of which was also missed by the Mantoux test with 1.0 mg. of old tuberculin. Two of the failures could not reasonably be ascribed to an insufficiency of the patch test, but rather to the biological character of the tuberculous condition, miliary tuberculosis, and positive anergy. From this survey, the tuberculin patch test appears to be sufficiently reliable for case finding.

Because of the rapid deterioration of old tuberculin and the cost of the purified protein derivative J. D. Craig and L. A. Scheuer compared the Vollmer patch test for the detection of tuberculosis. This test is more suitable for use by the general practitioner. A group of 212 children, known to be positive to 1.1,000 old tuberculin, were tested with the Vollmer patch test and the first strength purified protein derivative. Of these 95.1 per cent were positive to the Vollmer patch test and 84 per cent to the purified protein derivative. In the latter group negative reactions were usually found in those whose positive reaction to old tuberculin was not recent. The Vollmer patch test was the more sensitive if more than a year had elapsed since the old tuberculin test. The authors concluded that the patch test was a reliable method of diagnosis in tuberculosis.

Comparison of Tuberculin Patch and Mantoux Tests

A. J. Pearce *et al.* report on 712 school children who were given both the tuberculin patch test and the Mantoux test, first and second strength purified protein derivative. Of these 712 children, 616 had either both tests positive or negative, the percentage correlation between the two tests being 87 plus. Sixty-six had positive patch and negative Mantoux, and 21 had positive Mantoux and negative patch tests. It was concluded that the tuberculin patch test has a high degree of correlation with the Mantoux test and appears to give 7 per cent more positives than the latter. The tuberculin patch test is as reliable as the Mantoux, and the ease with which it is applied and its freedom from causing damage render it preferable to the Mantoux test. It appears, therefore, to be the best method for use in large scale tuberculin testing, especially for children.

Craig, J. D., and Scheuer, L. A. (1940) *Arch. Pediat.*, **57**, 177.

Pearce, A. J., Fried, R. I., and Glover, V. A. (1940) *J. Amer. med. Ass.*, **114**, 227.

Vollmer, H. (1940) *J. Pediat.*, **16**, 627.

Treatment

Sulphonamide Compounds

K. Birkhaug investigated the effect of sulphonamide, given parenterally, on the development of experimentally induced bovine tuberculosis in guinea-pigs. From

the clinical study of the animals, the survival rate, and the findings at necropsy, he concluded that sulphonamide inhibited the development of the infection.

H. J. Corper *et al.* also investigated the effect of sulphanilamide in guinea-pigs infected with virulent human bacilli. Large doses of the drug over long periods of time, parenterally as well as orally, and begun before or coincidentally with the infection, had an apparent, though not real, effect upon the organic tuberculous involvement of these animals, particularly in the spleen. The apparent effect is explainable as an organic toxic effect of the drug, since it can also be noted when heat-killed and avirulent human tubercle bacilli are given intravenously in large amounts to animals which are treated as compared with untreated controls. Even in large doses the drug has no appreciable effect on the spread of tuberculosis in guinea-pigs infected by various routes and in various ways with virulent human tubercle bacilli, such an effect as is observed can be entirely explained on the basis of the toxic effect of the drug, not upon a retardation of the disease.

Birkhaug, K. (1939) *Brit. med. J.*, **2**, 54.

Corper, H. J., Cohn, M. I., and Bower, C. (1939) *Amer. J. Tuberc.*, **40**, 452.

TULARAEMIA

See also B.F.M.P., Vol. XII, p. 309; and Surveys and Abstracts 1939, p. 582.

Treatment

Sulphanilamide

W. I. Curtis reported the case of a middle-aged woman who, eight days after handling dressed rabbits, developed the signs and symptoms of acute tularemia. She had fever, nausea, headache, vomiting, and an ulcer on the right middle finger. For a fortnight her condition, which was at first thought to be influenza, grew worse, her afternoon temperature rising to 104° F. She was given sulphanilamide in a dosage of 15 grains, four times a day, and in 2 days she recovered, although the drug was continued until she had taken 210 grains. Blood-examination confirmed the diagnosis of tularemia.

Curtis, W. I. (1939) *J. Amer. med. Ass.*, **113**, 294.

TUMOURS

See also B.E.M.P., Vol. XII, p. 313, and Surveys and Abstracts 1939, p. 583.

Diagnosis of Malignancy

Sternal Puncture

Rohr and Hegglin (1936) and other workers found the examination of the bone marrow obtained by sternal puncture of value in the diagnosis of malignant disease. I. Kreyberg and L. Poppe investigated 100 cases of malignant disease. Sternal biopsies and smears were made in all cases. The sections were found to be more reliable than the smears. In 8 cases malignant cells were found in the specimens, and all these were in the last stages with widespread metastases. In some cases the origin of the tumour cells, and therefore the site of the tumour, can thus be diagnosed.

Kreyberg, L., and Poppe, E. (1940) *Lancet*, **1**, 593.

Rohr, K., and Hegglin, R. D. (1936) *Dtsch. Arch. klin. Med.*, **179**, 61.

Interaction *in vitro* of Fibroblasts and Sarcoma Cells with Leucocytes and Macrophages

In an elaborate and technical paper R. J. Ludford reports an experimental research by tissue culture, carried out in the laboratories of the Imperial Cancer Research Fund, on the interaction *in vitro* of fibroblasts and sarcoma cells with leucocytes and macrophages. Carrel's tissue-culture work led him to the conclusion that leucocytes secrete substances ('trephones') *in vitro* which promote cell multiplication. Ludford's work confirms the work of Carrel in demonstrating that cultures of

leucocytes produce substances which stimulate the growth of fibroblasts and sarcoma cells. The following are Ludford's other conclusions. When fibroblasts and sarcoma cells were grown together with leucocyte cultures, their growth began sooner, and was ultimately more extensive than when they were grown alone. Growth stimulation occurred without actual contact between the two types of cells. When fibroblasts or sarcoma cells were grown in contact with the cells from leucocyte cultures, not only was the growth of the former stimulated, but also their capacity to digest clotted plasma (proteolysis). In mixed culture both kinds of cells remained in a more active functional state. On the assumption that the same cellular reactions occur in the animal body as have been described in tissue cultures, the author suggested that monocytes and macrophages, by stimulating the growth and proteolytic activity of malignant cells, may facilitate their invasive growth into normal tissues.

Carrel, A. (1922) *J. exp. Med.*, **36**, 385.

(1927) *C. R. Soc. Biol., Paris*, **97**, 19.

Ludford, R. J. (1940) *Brit. med. J.*, **1**, 201.

Sarcoma of Popliteal Space

R. Desjaques reported a case of sarcoma of the popliteal space occurring 21 years after a wound in this area, in which a small fragment of needle had been left. There had been no difficulty in the intervening period. The tumour was diagnosed as a polymorphous sarcoma, and amputation was carried out in the middle third of the thigh. The patient died of metastases about one year later.

Desjaques, R. (1939) *Rev. Chir., Paris*, **58**, 373.

TYPHUS FEVERS

See also B.I.M.P., Vol. XII, p. 325, Cumulative Supplement, Key Nos. 1558-1560, Surveys and Abstracts 1939, p. 583, and p. 76 of this volume.

Epidemiological and Clinico-pathological Considerations

M. Daniëlopolu *et al.*, with much experience since 1916 in Moldavia, in Bucarest in epidemics in war and small endemic foci in peace, report some of their conclusions. The incubation period in the past has been variously estimated as from 5 to 20 days, in epidemics adults show an average incubation of 8 days, this was the interval between a single bite by an infected louse and the onset of illness in medical attendants and nurses who were not infested by lice. The shortest period was 7 days, this was the case in the severe 'hypertoxic' form seen in the war epidemics. In slight, abortive forms occurring at the beginning and end of epidemics and in endemic outbreaks the incubation period may be much longer, in adults 14 days. The typhus seen in the epidemics of war is regarded as the complete form of the disease, the other forms as incomplete. Typhus running its course in 15 days is divided into the slight, the average, and the hypertoxic forms. The infection is conveyed by body lice, not by head lice, as has been suggested. Relapsing fever is also conveyed by body lice, and epidemics of typhus and relapsing fever may occur at the same time. The usual way of infection is by the bite of an infected louse, though in some instances, especially in winter, the dejecta of infected lice may carry the infection through abrasions of the skin, due to scratching, into the circulation and so transmit the disease. Stress is laid on the localization of the infective agent on the walls of the small blood vessel thus causing the rash, fall of blood-pressure, fatal myocardial changes, blood cells in the urine, and haemorrhages in the central nervous system.

Blood Changes

In slight forms of typhus, leucocytosis is small; in the average form the leucocytosis of about 20,000 may persist for some days after the temperature has become normal. In the hypertoxic form the count tends to be higher, 50,000, 60,000, or 80,000, the highest count made by the authors was 126,000. In most cases the increase was in the mononuclears, there were constantly 2 abnormal elements in the blood, namely, a plasma cell with a basophilic protoplasm and a monocyte derived

from the reticulo-endothelial system. The degree of the leucocytosis and the number of these cells ran parallel with the severity of the disease. In secondary streptococcal infections, which are specially prone to occur in typhus, such as otitis, parotitis, erysipelas nearly always round the nostril, quinsy, and subcutaneous abscesses, the leucocytosis is polymorphonuclear.

Cerebrospinal Fluid

Examination was made of 150 patients. There was always a leucocytic reaction due to meningeal and vascular lesions, with mononuclear polymorphonuclear, plasma, and red blood cells, the cell count rising with the severity of the case.

Prophylaxis

As de-lousing may be difficult in war conditions, the use of a vaccine of the virus of murine typhus, as practised by G. Blanc and Laigret, is recommended.

Daniélopou, M., Lupu, M., Ciaciun, I., and Petresco, M. (1940)
Bull. Acad. Méd. Paris, **123**, 56.

Non-Epidemic or Epizootic Fevers

Mite-Typhus

Tsutsugamushi. —R. Lewthwaite and S. R. Savor. The rickettsia diseases of Malaya with special reference to tsutsugamushi disease. The typhus-like fevers of British Malaya are not louse-borne and do not flare up in epidemics. In the last 10 years, the authors examined 250 patients with tsutsugamushi and are convinced that the disease is identical with rural or scrub typhus. The condition is common in Japan and is spread by a larval trombidid. Its initial dermal lesion is at the site of the bite, and may not be more than a papule, in only 44 of the 250 cases did it develop into an ulcer; there is also attendant bubo. Rural or scrub typhus is said to show neither the lesion nor the bubo. There can be no doubt that the alleged absence of the lesion is due to its early and insignificant appearance, and to the dark skins of so many of the sufferers. Otherwise, clinically and pathologically the two diseases are identical and the results of cross-immunity tests support this view. The authors consider that the name of rural or scrub typhus should be abandoned, and that of tsutsugamushi retained.

Lewthwaite, R., and Savor, S. R. (1940) *Lancet*, **1**, 255, 305.

ULCERS

Chronic Undermining Ulcers

Treatment

Sulphanilamide. —K. B. Lawrence reports success from the use of sulphanilamide in a case of resistant chronic undermining streptococcal ulcer, in a girl, aged 15, who had sustained a floor-burn in the school gymnasium, the affected area was just below the left knee on the antero-lateral aspect of the limb. In spite of local treatment an ulcer with undermined edges and a central sinus formed. During 6 weeks before admission to hospital the ulcer remained in an indolent state, it was ovoid and measured 9.0 by 7.0 by 0.8 cm. The lateral margin was deeply undermined and discharging thin yellow-grey pus. Cultures obtained showed an anaerobic haemolytic streptococcus, *S. aureus* and *S. albus*. Wet saline and Dakin's solution dressings exerted some cleansing of the ulcer bed, but the ulcer did not get smaller. One month after admission zinc-peroxide paste dressings were applied; healthy granulations then appeared and normal epithelium began to grow in from the margins. Progress was so favourable that the area was pinch-grafted, but 8 days later the grafts liquefied, and there was an exacerbation of the infection in the ulcer bed. Response to X-ray therapy was also unfavourable. Four months after admission sulphanilamide therapy was begun, and continued for about 3 months. The dosage ranged from 80 to 100 grains daily in divided doses, together with sodium bicarbonate. The ulcer healed gradually, the response to the drug being very convincing. The sulphanilamide level ranged from 0.5 to 3.4 mg. per 100 c.cm. A total of 8,400 grains was given. Healing was complete.

Zinc peroxide—T. A. Shallow *et al.* employed zinc peroxide in 6 cases of chronic undermining burrowing ulcers due to the micro-aerophilic haemolytic streptococcus. These cases had gone on for indefinite periods unrecognized as to aetiology, and not responding to various methods of treatment. When, however, potent freshly prepared zinc peroxide cream was carefully applied to all affected parts, and protected against drying, the effect was dramatic. Within a few days the exudation ceased, granulations began to fill in, the undermining became less, and the wound took on a healthy appearance.

Zinc peroxide and sulphanilamide—F. L. Melency and H. D. Harvey treated 18 cases of chronic undermining burrowing ulcer with zinc peroxide locally and sulphanilamide by the mouth. In addition they treated one case with sulphanilamide alone and another with zinc peroxide alone. The ulcers were due to the micro-aerophilic haemolytic streptococcus. The organism is usually found beneath the undermined skin flap. After a few transplantations the organisms are indistinguishable from Group A haemolytic streptococcus. This led the authors to try sulphanilamide in the treatment of the condition.

Zinc peroxide powder suspended in distilled water in the proportion of 40 per cent to form the consistency of cream should be closely applied to the wound. The dressing should be changed every day and not allowed to evaporate. At the same time 1-2 g. of sulphanilamide should be given by mouth every 4 to 6 hours. If any toxic symptoms appear the drug should be stopped. If the ulcer is still active after a week, surgical treatment is necessary to bring the infected part into contact with the zinc peroxide. Treatment is then continued as before. After another week the surgical attack is repeated if necessary. When the area is covered with granulation tissue it is skin-grafted and almost 100 per cent successes may be expected. The two control cases treated with sulphanilamide or zinc peroxide alone both healed. In 8 cases the sulphanilamide was given before the zinc peroxide, producing a beneficial result in only one case. In 8 other cases the drugs were given together with beneficial results to 3. In the other 5, toxic reactions to the sulphanilamide occurred, and in 3 of them they were serious. The 2 remaining cases received sulphanilamide some time after the zinc peroxide. One of them improved greatly but in the other the drug had to be stopped owing to toxic reaction.

The authors concluded that sulphanilamide alone will cure the condition but that it takes longer than either zinc peroxide alone or a combination of the two treatments.

Lawrence, K. B. (1940) *New Engl. J. Med.*, **222**, 573.

Melency, F. L., and Harvey, H. D. (1939) *Ann. Surg.*, **110**, 1067.

Shallow, T. A., Fry, K. E., and Pulaski, E. J. (1940) *Surg. Gynec. Obstet.*, **70**, 987.

UMBILICUS DISEASES

See also B. L. M. P., Vol. XII, p. 352

Infections

Diphtheria

A. R. Thompson reported a case of diphtheritic infection of the umbilicus in an infant aged 19 days. The umbilicus became inflamed and moist, and a necrotic area developed in the middle which finally separated, the lesion healed with hardly any scarring. During this time the baby's general health and weight remained good. There was no sign of faucial diphtheria, but the nares were crusted and inclined to bleed on swabbing. Eight or 9 days after the beginning of infection, a direct smear from the umbilicus was diphtheria-positive, although the organism was atypical. The infant was given a total of 50,000 units of diphtheria antitoxin, and local magnesium sulphate and glycerin paste and a 2 per cent solution of potassium tellurite were applied locally. Five days after admission the patient developed a doubtful left ptosis, followed by a transient squint and a flaccid attitude with loss of tendon reflexes. These manifestations disappeared, however, and the baby was discharged well and Schick-negative about 12 weeks after admission. The mother

of the baby was strongly Schick-positive and the father slightly so at the time of admission to hospital.

Thompson, A. R. (1939) *Brit. J. Child. Dis.*, **36**, 171.

UNDULANT FEVER

See also B.E.M.P., Vol. XII, p. 361; and Surveys and Abstracts 1939, p. 584.

Diagnosis

Serum-Agglutinin Test

V. Badoux states that the sero-agglutination, as practised in all laboratories for the diagnosis of undulant fever, is quite insufficient. Examining 62 cases suspected of the disease the author obtained 7 positive results by the agglutination method, and 14 positive results by the complement-fixation method. These 14 cases were also diagnosed clinically as undulant fever.

Badoux, V. (1939) *Schweiz. med. Wschr.*, **69**, 1245.

Clinical Picture

Vertebral Lesions

W. A. Bishop stated that arthropathies occurred during the active period of undulant fever because then septicaemia was present. Disease of the spine is the most common bone and joint complication in this condition. The bone lesions may be due to any of the 3 sub-species of the brucella group. Of 56 cases of spondylitis reported 40 were in the lumbar region, 10 in the thoraco-lumbar, 4 in the thoracic, and 2 in the cervical. The condition may be acute or chronic, the former simulating acute osteomyelitis, and in the latter bony spurs appear usually on the anterior surface of the vertebral bodies. X-ray examination shows sclerosis in the affected bones. Later intense calcification takes place and the bony spurs form. Pain and spinal rigidity occur and abscesses may form. The condition is diagnosed by the history, X-ray examination and the positive response to specific tests for undulant fever. The primary disease should be treated and the spine supported during convalescence. Abscesses may require drainage. Most cases recover. Bishop reported a case in which *Brucella suis* was isolated from the blood-stream. The patient improved after treatment by surgical fusion to the lumbar region and support to the cervical region.

Bishop, W. A. (1939) *J. Bone Jt. Surg.*, **21**, 665.

Treatment

Sulphonamide Drugs

J. Kleeborg *et al.* reported 6 cases of undulant fever, treated with sulphonamide drugs. In 5 of the cases blood culture were positive, and in 4 skin tests were positive. The drug caused the temperature to drop at first and the blood cultures to become sterile in 5 cases, 2 during treatment and in the other 3 up to 78 days after the treatment was stopped. The drug did not, however, alter the clinical picture, even in one case which received a total of 44 g., and new rises of temperature occurred. Toxic effects in the shape of weakness, fever, and one case of orchitis occurred. It was therefore concluded that, as the prognosis is nearly always good in undulant fever and toxic reactions may arise from the treatment, sulphanilamide derivatives should be used with caution in this disease.

Vaccine Therapy and Sulphonamide Therapy

M. Lincoln employed a combination of vaccine therapy and neoprontosil with successful results in a case of undulant fever in a woman of 60 years of age who developed the disease following the consumption of raw milk. The treatment employed was as follows: the patient was given an injection of 0.07 c.cm. of undulant fever vaccine and as a result developed a violent skin reaction; 0.1 c.cm. of the vaccine was then diluted 17 times and she was given 0.1 c.cm. of this dilution. This gave a much smaller skin reaction. She was then given increasing doses at 3-day intervals for 3 weeks. In addition, following the second injection, a course of

neoprontosil by mouth was instituted; this consisted of 40 grains a day for 3 days, 30 grains a day for 4 days, and then 10 grains a day. At the end of 10 days she had no fever, malaise, or sweats, and she felt stronger. At the end of 3 weeks she appeared to be quite well, and her white blood-cell count was between 8,000 and 9,500. She continued to work throughout the entire illness. Eight months later she had had no recurrence, and an agglutination test for brucella was negative.

Kleeberg, J., Gurevitch, I., and Alkan, W. J. (1939) *Trans. R. Soc. trop. Med. Hyg.*, **33**, 169.

Incoln, M. (1940) *Northw. Med., Seattle*, **39**, 64.

URETHRA DISEASES

See also B. E. M. P., Vol. XII, p. 386, and Surveys and Abstracts 1939, pp. 156 and 584.

In Male

Meatal Stenosis

H. Dodd gives his experience of this condition which is seldom recorded, but is not rare, being seen in general surgical practice about once a month. The diagnosis is self-evident, but the difficulty is that this possibility is seldom considered. His 26 cases are divided into 3 groups (*a*) infants and boys (11) with diagnoses such as phimosis, bilateral hydroceles, difficult micturition, nocturnal enuresis, pain in the right iliac fossa, appendicitis, and right inguinal hernia, (*b*) adults up to 55 years of age (8) presenting lumbago and sciatica, perineal pain, pain in right iliac fossa, appendicitis, enlarged prostate, (*c*) the prostatic age, 55 upwards (7) with symptoms of prostatic enlargement, recurrent piles. The treatment is incision, no amount of stretching, which is very painful, is effective. It is performed under local anaesthesia by 2 c.c. of 0.5 per cent solution of novocain. The after treatment is simple, the patient goes about immediately, a small piece of gauze is loosely laid over the part and acriflavine is trickled on morning and evening.

Hypertrophied Verumontanum

J. L. Emmett records the case of a male child aged 1½ years, with obstruction of the neck of the urinary bladder by a hypertrophied verumontanum, an unusual condition described by H. G. Bugbee and M. Wollstein (1923). The patient had increasing difficulty in micturition, slight pyuria, blood urea 15 mg. per 100 c.c., haemoglobin 11.6 g. per 100 c.c., and a leucocyte count of 12,000. The diagnosis was made by the MacCarthy miniature cystoscope with the number 15 French sheath, there was not any evidence of cystic change in the verumontanum which occluded the urethra almost completely. Treatment by fulguration was successful, an electrode being passed through the cystoscope. This was carried out before serious damage was done to the urinary tract by the obstruction.

Bugbee, H. G., and Wollstein, M. (1923) *J. Urol.*, **10**, 477.

Dodd, H. (1940) *Med. Pr.*, **211**, 121.

Emmett, J. L. (1940) *Proc. Mayo Clin.*, **15**, 364.

In Female

Urethritis Follicularis

Inadequate description and evaluation has appeared in the literature of the nodular or polypoid protrusions often found at the proximal portion of the female urethra and bladder neck, the so-called urethritis follicularis. Because of the obviously benign character of these lesions, they have seldom been subjected to biopsy. I. J. Zimmerman reports on the microscopical appearances of follicular urethritis, as shown on examination of the nodules removed from the urethras of 3 women, in the third, fourth, and fifth decades respectively. In all the 3 women infection of the uterine cervix, and pus and bacilli in catheter specimens of urine were present, two had cystoceles with incontinence, and the third a papilloma of the bladder with a right-sided pyelonephritis, presumably associated with mild obstruction caused by the papilloma. The biopsy in each case revealed a solitary lymph follicle with densely

packed lymphocytes at the periphery and a typical germinal centre. The lesion is not confined to the female urethra; its occurrence in a man of 66, with severe bacillary infection secondary to an infected hyperplastic prostate is described. Aetiologically these nodules are apparently secondary to infection elsewhere in the genito-urinary tract, although coexisting anatomical or physiological factors probably play an associated part.

Tumours

Carcinoma—A. M. Sala and N. M. Levine report 2 cases of carcinoma of the female urethra. The condition is rare, only about 262 cases having been previously recorded. Although the average age of the collected cases is 54, and there is usually a history of a pregnancy or pregnancies, one of the 2 patients was a nullipara, aged 34. The condition is suggested by the presence of stricture and of a palpable mass. The essential diagnostic procedure is adequate biopsy, preceded by thorough local examination.

Sala, A. M., and Levine, N. M. (1940) *Urol. cutan. Rev.*, **44**, 62.
 Zimmerman, I. J. (1940) *New Engl. J. Med.*, **222**, 221.

URINE EXAMINATION

See also B.F.M.P., Vol. XII, p. 393; and Surveys and Abstracts 1939, p. 585.

Albumin and Blood

Occult Haematuria

J. H. Barach and L. L. Pennock tested 3,000 specimens of urine from 681 ambulatory patients for occult haematuria. The patients were those with cardiac, renal, nutritional, and other chronic diseases. Cases of gross haematuria were not included in the series. The haematuria was detected by the toluidine test. In a third of the cases the reaction was positive. Occult haematuria was commoner in women than in men, and in the old rather than the young. This is probably due to bleeding from the uterus in females, and the greater vulnerability of blood vessels in the old. Glycosuria, arsenic therapy, and the reaction of the urine had not any influence on the incidence of haematuria. It was commoner in summer than at any other season. Those in whom the condition was persistent often showed hypochromic anaemia. The reaction is an index of the patient's general condition, and is most often positive in those more seriously ill.

Barach, J. H., and Pennock, L. L. (1940) *J. Amer. med. Ass.*, **114**, 640.

Chemical Constituents

Urinary Amylase Estimation

Diagnostic significance.—D. L. Dorzi reports on an investigation of the significance of urinary amylase, the normal range of which varies considerably. The urinary amylase was studied in patients with diabetes mellitus, nephritis, thyrotoxic disease, hepatic and pancreatic diseases. High and low figures were obtained in each group. The highest figures were in patients with pancreatic disease, but the findings were not consistent. As a result of the great variations in normal patients, and the lack of consistent findings in these diseases, it was concluded that the routine use of the determination of urinary amylase for diagnostic purposes did not give significant results.

Dorzi, D. L. (1940) *Amer. J. digest. Dis.*, **7**, 123.

Tests of Renal Function

One-Hour Renal Condition Test

W. G. Lixton and A. R. Rose describe a one-hour renal condition test which determines the function and organic status of the glomeruli and tubules. This test is

specially useful in finding the cause of unexplained albuminuria. It has been shown that all the nephrons in the kidney do not function at the same time, but that groups of them function in rotation. In one hour, however, all the nephrons have functioned. A one-hour urine analysis therefore gives a complete picture of the functional activity of the kidneys. For 15 hours before the test the patient should leave off medicine or alcohol, take as little fluid as possible, and for 3 hours before the test the patient takes no fluid at all. The basal hour begins immediately after the patient empties the bladder and ends when he begins to fill the bladder. The first sample of urine is discarded and the second measured and analysed. The patient should be at rest during that hour, but in some cases a second test, carried out during an hour of activity, is necessary. If albumin or globulin is present in the specimen, the amount determined may be used to calculate the amount of kidney damage, since it is known that all the nephrons have functioned in the hour. The number of casts, red cells, and white cells excreted per hour also gives a good idea of the degree of damage in renal disease. Exton and Rose report 8 cases of urinalysis illustrating this method.

Exton, W. G., and Rose, A. R. (1940) *Amer. J. clin. Path.*, **10**, 73.

UROGENITAL ORGANS, ABNORMALITIES

See also B I M P, Vol. XII, p. 401, and Surveys and Abstracts 1939, p. 586.

Urethra

Hypospadias

Surgical treatment. In discussing the surgical treatment of hypospadias, C. M. McKenna stresses the importance of correcting the ventral curvature of the penis before attempting reconstruction of the urethra. For if this is not done normal erection may be impossible. Operation should not be undertaken until the parts are large enough to make surgical manipulation relatively easy. About 12 to 14 years is the best age, but the curvature may be corrected a year or two earlier. If the genitalia are small, testosterone propionate may be used to aid their development. Before operation is undertaken urinary drainage by suprapubic cystostomy should be established. Skin to be used for construction of the urethra should first have all its hair follicles destroyed by electrolysis. Unless this is done a successful operation may be spoiled by hair inside the urethra constantly becoming encrusted. The suitable method for reconstruction of the urethra varies in different cases. In all cases there should be no tension on the graft used to make the tube, and skin clips should be used in preference to sutures. If oedema occurs clips do not cut through so easily as do fine sutures and therefore do not leave a tract which favours the formation of fistulae. If small fistulae occur in spite of great care a pedicle flap from the scrotum may be used to cover the bare area.

McKenna, C. M. (1939) *J. Amer. med. Ass.*, **113**, 2138.

True Hermaphroditism

A. K. Doss and J. T. Priestley reported a case of true hermaphroditism in which bilateral ovotestes were present. The total amount of gonadal tissue was composed almost equally of ovarian and testicular structures. The external genitalia appeared grossly more those of a male than a female. The secondary sex organs found consisted only of a Fallopian tube on each side and a rudimentary vagina. The breasts were somewhat enlarged. There was no evidence of a cervix or of a uterus. There was a rudimentary epididymis on one side. No definite evidence was present of a prostate gland, seminal vesicles, or verumontanum. The child was transformed by operation into as complete a male as possible by removal of all female structures, and the preservation of all male structures.

Doss, A. K., and Priestley, J. T. (1940) *J. Urol.*, **43**, 859.

UTERUS, DISEASES AND DISORDERS: DEVELOPMENTAL ABNORMALITIES

See also B.E.M.P., Vol. XII, p. 416; and Surveys and Abstracts 1939, p. 587.

Hereditary Absence of the Uterus

P. Delbet records this defect in 5 women in 3 generations of the family. In all the secondary sex characters were highly developed, they were all married, and had not any symptoms of menstrual disorder. It was assumed that the ovarian hormones were normally present, and that there was complete absence of the uterine mucosa.

Delbet, P. (1940) *Bull. Acad. méd. Paris*, **123**, 176.

UTERUS, DISEASES AND DISORDERS: TUMOURS

See also B.E.M.P., Vol. XII, p. 448, and Surveys and Abstracts 1939, p. 588.

Adenoma of Cervix Uteri

Hyaline Adenoma

N. W. Elton reported a case of hyaline adenoma of the cervix and 2 other cases simulating this condition, all in multiparae. In the first case the patient had undergone hysterectomy for diagnosed adenocarcinoma. Two years later a polypoid growth of the cervix was removed, it showed proliferating cervical glands enclosed in a dense hyaline stroma. The glandular epithelium showed squamous metaplasia. Further biopsy showed atrophy of the glands with islands of squamous epithelial tissue and even more extensive hyaline change in the stroma. There was no evidence of malignancy. The two other cases were similar, but the hyaline stroma was absent, and in one of them multiple fibroids were also present. The condition was thought to be inflammatory.

Elton, N. W. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 121.

Endometrial Mole-Type Tumours

Aetiology

H. Selye and S. Friedman found that the uteri of post-pubertal ovariectomized rats treated with daily doses of 100 μ g (0.1 mg.) of oestradiol, 3 mg. of testosterone propionate, or 3 mg. of pregnenolone were sensitized to local trauma in such a manner that gelatinous tumours of the endometrial mole type developed at the site of injury. No such tumours were produced in the traumatized uteri of untreated control animals. These observations gave further support to the conception that both local injury and an appropriately prepared humoral medium are essential for tumour production.

Selye, H., and Friedman, S. (1940) *Amer. J. Cancer*, **38**, 558.

Mixed Mesodermal Tumours of Uterus and Vagina

A. L. Amolsch reviews the subject of heterotopic mesodermal tissue tumours of the uterus and vagina and describes 6 examples, one of the vagina, 4 of the cervix, and one of the body of the uterus. These remarkable tumours have been given various names; McFarland tabulated 116 terms that have been used to describe neoplasms which on the basis of microscopic structure may reasonably be included in one class, and suggested the designation dysontogenetic tumour. They may be benign, as in the case of the rare lipoma of the uterus, more often they are complex in tissue composition and malignant; but the latter character may not be recognized until recurrence appears. Among 447 recorded cases remote metastases were recorded in 14, and the mortality rate for all the reported cases is more than 95 per cent. They are specially prone to recur and extend locally. Parity had not any influence on the development of these tumours; of the vaginal tumours 60 per cent occurred in the first 2 years of life; 30 per cent of the tumours of the body of the uterus and 60 per

cent of the cervical tumours in nulliparae. The average age incidence of tumours of the body of the uterus was 55 years, of cervical growths 31 years, and of vaginal neoplasms under 22 years, 60 per cent being under 2 years. The tumours are relatively resistant to radiological treatment. The symptoms are much the same as those of uterine myoma or carcinoma, but may not appear until the polyp has reached a fair size. Simple removal is inadequate, a wide hysterectomy and intensive radiological treatment are recommended. In all the author's cases the tumours contained myxomatous tissue which, being an embryonic structure, should, in the absence of other evidence of a mixed mesodermal tumour, be regarded as such and action taken as for a malignant growth.

Amolsch, A. L. (1939) *Amer. J. Cancer*, **37**, 435.

McFarland, J. (1935) *Surg. Gynec. Obstet.*, **61**, 42.

Carcinoma of the Cervix Uteri

Occurring Before the Age of Twenty

A. W. Diddle stated that available literature revealed 18 reports of cancer of the cervix uteri occurring before the age of 20. Of these cases, 3 were designated as epitheliomas, 9 as adenocarcinomas, and in 6 the type was not indicated. Five cases occurring under the age of 14 were adenocarcinomas. Of the 18 cases, 6 died within a year. The impression was gained that the prognosis of cancer of the cervix before the age of 20 is grave, because of the accelerated growth impulse in malignant tumours during the years of growth.

Effect on Urinary Tract

H. S. Everett reports observations on the effect of carcinoma of the cervix and its treatment upon the urinary tract. Forty-six patients were examined urologically before treatment was given, 17 of these were subsequently re-examined after irradiation therapy, together with 16 others of whom there had been no preliminary examination. He found that, if there were lesions in the upper urinary tracts before treatment, the prognosis was very grave. About 50 per cent of the patients showed some obstruction involving the lower ureters with dilatation of the pelvis of the kidneys and of the ureters above the point of obstruction, as the result of irradiation. In only about 15 to 20 per cent was this lesion serious, but it was considered advisable to examine urologically all patients receiving irradiation treatment for carcinoma of the cervix.

Treatment

Interstitial radium. H. C. Pitts and G. W. Waterman report on 135 cases of cancer of the cervix uteri treated by interstitial radium, and followed up for a period of 5 years. They also included the results obtained with a previous group of 173 cases similarly treated. Deducting 19 cases too advanced to treat, 11 cervical stump cases, and 14 cases treated elsewhere with radium and/or X-rays before coming under the authors' observation, there was a relative survival rate of 95 out of 264, or 36 per cent.

Carcinoma of Corpus Uteri

Adeno-acanthoma

H. J. Schattenberg and J. Ziskind report a case of adeno-acanthoma of the uterus. The tumour consists of groups of adenocarcinoma and areas of squamous epithelium. It probably arises as a metaplastic change in the cylindrical cells of an adenocarcinoma of the body of the uterus. The prognosis is correspondingly worse, approaching that of carcinoma of the cervix. The tumour occurred in a multipara, aged 42 years, who had pain in the right side of the abdomen, nausea and vomiting, a purulent vaginal discharge for 5 months, irregular action of the bowels, and urinary frequency and nocturia for 3 months. Thirteen years before admission she had been successfully treated for vaginal haemorrhage by curettage. Before admission she had menorrhagia and metrorrhagia for some months. The patient was anaemic and a fungating mass was felt in the cervix. She was treated with transfusions and infusions, and deep X-ray therapy to the pelvis was started. About 2

months later pan-hysterectomy was performed. Her general condition was poor and she died 5 days after operation. No metastases were found at the necropsy.

Diddle, A. W. (1940) *Amer. J. Cancer*, **39**, 207.

Everett, H. S. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 889

Pitts, H. C., and Waterman, G. W. (1940) *Amer. J. Roentgenol.*, **43**, 567.

Schattenberg, H. J., and Ziskind, I. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 112

UVEAL TRACT DISEASES

See also B. L. M. P., Vol. XII, p. 495, and Surveys and Abstracts 1939, p. 590

Tuberculous Kerato-iritis

Treatment

Beta-rays of radium A. C. Woods treated 10 cases of tuberculous kerato-iritis and 3 cases of deep tuberculous scleritis with beta-rays of radium. Two other patients were treated, but the results could not be followed up. The dosage varied from 1 g. for 3 seconds every 3 weeks to larger doses of 1 g. for 12 seconds at not less than 2 weeks' interval. The total dose depended upon the condition treated and the response. These doses are for 1 area only, multiple areas on one eye or one cornea may be treated at one sitting. Light of the patients suffering from kerato-iritis recovered after one course of treatment, but in the other 2 there were recurrences. The cases of deep scleritis responded much more slowly than those of kerato-iritis. One patient was improved and finally cured after 8 months' treatment. Another patient improved after 2 years' treatment, but in the third case improvement was only temporary, the patient relapsing after she had returned home. The relatively poor results in the case of scleritis may be because the sclera is not so permeable to the rays as the cornea. All the patients also received the usual local and general treatment for their condition. The rays are thought to act by bacteriostatic action or abiototic action on the causal organisms or by stimulating the production of immune bodies. It was stated that the effects of the irradiation may only last a few months but there is no harm in repeating the treatment after that time.

Woods, A. C. (1939) *Arch. Ophthalmol., N. Y.*, **22**, 735.

VACCINIA AND VACCINATION

See also B. F. M. P., Vol. XII, p. 515; and Surveys and Abstracts 1939, p. 590.

Vaccination

Effect of Human Convalescent Serum on Vaccination of Infants

J. Greengard and A. M. Wolf investigated the effect of human vaccinia convalescent serum on the vaccination of infants. The serum was obtained from adults who had recently been successfully vaccinated. Thirty-six unvaccinated infants up to 1 year of age were investigated. They were given 10 to 20 c.c. of the serum, 24 hours before vaccination. The serum proved to have a strong specific action. On vaccination only 38 per cent of infants so treated showed typical takes. Of 35 controls, 71 per cent were successfully vaccinated. The serum must be introduced intravenously and be given before the virus has entered the cells. It has been found that, as in all virus diseases, to be effective the antibody must reach the healthy tissue before the virus does.

Comparison of Rivers's Culture Virus and Calf-Lymph Virus

H. H. Donnelly *et al.* made a comparative study of intradermal and cutaneous vaccination with Rivers's culture virus and with calf-lymph virus in newly-born infants. Cutaneous and intradermal vaccination with calf-lymph virus, undiluted and diluted 1:100 respectively, yielded the same percentage (93) of 'takes'. Intradermal vaccination with Rivers's culture virus gave 80 per cent of successful 'takes'.

Cutaneous vaccination with culture virus mixed with sterile egg white, desiccated and rubbed into the skin scratches yielded 'takes' in only 10 per cent of cases. The cutaneous reaction and invasiveness of the virus, indicated by lymphadenopathy, were practically identical with the culture virus and the diluted calf-lymph when both were employed intradermally. Intradermal use of both preparations gave mild cutaneous lesions in newly-born infants.

Donnelly, H. H., Nicholson, M. M., Anderson, W. S., and Grosvenor, M. H. (1940) *Amer. J. Dis. Child.* **59**, 322
Greengard, J., and Wolf, A. M. (1940) *Amer. J. Dis. Child.* **59**, 76.

VEIN DISEASES

See also B.I.M.P., Vol. XII, p. 526. Surveys and Abstracts 1939, p. 591, and pp. 13 and 137 of this volume

Varicose Veins

Aetiology

J. C. Adams, investigating the aetiological factors in varicose veins of the legs, employed direct venous pressure determinations in the saphenous vein. He concluded that the erect posture has resulted in venous pressure in the leg which may reach 100 mm. Hg. depending on the height of the patient. The erect posture has developed activity stresses which markedly increase intra-abdominal pressure and raise the saphenous pressure indirectly to unusual heights. Combined with a vulnerability in certain individuals, this is probably sufficient to produce varicose veins. Pressure readings before and after ligation suggested that the pressure factor, apart from the pure gravity effect, can be largely relieved by proper ligation of the saphenous vein. Unless preliminary ligation has been carried out, recanalization may be expected in incompetent veins, but it is unlikely if ligation has obviated the increased pressure effect of strain and the reverse flow in the saphenous vein.

J. I. Edwards and E. A. Edwards examined histologically the valves in the upper ends of varicose saphenous veins, and also, for comparison, the valves of normal veins. Most of the varices were either spontaneous in origin, or followed phlebitis of the deep veins. In these two groups of varices the valve cusps did not show any remarkable intrinsic lesions. The fundamental lesion was a dilatation of the commissural region, i.e. the portion of the wall between the attachment of the valve cusps. This gives rise to evagination of the wall and a separation of the cusps. Secondary reparative changes are growth of fibromuscular tissue on the internal surface of the dilated commissure. Intrinsic changes due to the primary lesion of the venous wall are relaxation of the cusp with redundancy and kinking, occasionally rolling of the free margin, and, in severe cases, a distal eversion of the cusp. So-called normal veins show early changes similar in nature to those present in varicose veins. The authors conclude that regurgitation of the blood in the upper saphenous vein, in the usual form of viscosity, is secondary to a relative insufficiency of the valves, depending on dilatation of the vein wall, and that the aetiology of varicose veins was to be sought in the disproportion between the venous pressure and the resistance of the vein wall. The usual type of varicosity is not due to local infection or inflammation, thrombophlebitis, or spontaneous degeneration of valves.

Treatment

Injection therapy. G. Delater and J. Delater claimed a high percentage of good results from the following technique employed for the obliteration of varicose veins. A mixture consisting of 1 to 2 c.cm. of 40 per cent sodium salicylate, 0.5 to 1 c.cm. of 40 per cent sodium benzoate, and 1 to 2 c.cm. of sodium morrhuate, 5 per cent, is injected at the first treatment; 4 to 5 injections can be given. The quantities may be increased at subsequent injections. As a rule the injections are painless. In resistant cases a mixture consisting of 3 to 5 c.cm. of glycerin, 2 to 3 c.cm. of 30 or 40 per cent sodium salicylate, and 1 to 3 c.cm. of sodium benzoate, may be employed. The mixture should be homogeneous.

High division and retrograde injection. - J. B. Sears and S. S. Cohen review the end-results of the treatment of varicose veins by high division and retrograde injection; 135 extremities in 87 patients were studied. In 29 extremities (21.4 per cent) there was complete freedom from varicose veins. In 81 extremities (60 per cent) the great saphenous vein system was entirely thrombosed, but there was some dilatation and stagnation in the tributary veins, or segments of the latter. In 25 extremities (18.5 per cent), which were considered as failures, a greater or lesser portion of the great saphenous vein was patent. The authors conclude that the combination of high ligation and retrograde injection is a satisfactory and valuable method of treating marked varicosity of the saphenous system.

Reactions after sodium morrhuate. - I. Dobson reported 2 cases in which severe reactions occurred after the use of 5 per cent sodium morrhuate for varicose veins. In one case the patient developed an urticarial rash on the forearms with tingling and burning of the palms. After another injection he became cyanotic and then went into coma. His pulse was rapid and weak and his blood-pressure fell to 50/40 mm. Hg. The other patient had symptoms of pruritus and oedema of the lips. In both cases the patients had had several previous injections without reactions.

Factors in recurrence. - L. K. Stalker and W. W. Heyerdale discussed the factors in the recurrence of varicosities following treatment. Recurrence often follows the injection of sclerosing fluids and even occurs after combined division and ligation of the great saphenous vein at the saphenofemoral junction. The first treatment fails because in the condition of varicosity the valves in the great venous systems are also deficient. Any rise of pressure is not held back in these veins and is passed on to the smaller veins in the leg. This causes the thrombus resulting from the sclerosing fluid to give way. The operative treatment fails because of lack of recognition of various anatomical considerations. Three tributaries distal to the entrance of the femoral vein into the saphenous vein must be ligated. Similarly, any superficial femoral veins present should also be ligated. If these measures are not taken, shunting of blood through the tributaries will occur and varicosities reform. The same factor applies in recurrence after stripping and excision of a segment of the vein.

Adams, J. C. (1939) *Surg. Gynec. Obstet.*, **69**, 717.

Delater, G., and Delater, J. (1940) *Pr. med.*, **48**, 54.

Dobson, I. (1940) *Ann. Surg.*, **111**, 645.

Edwards, J. F., and Edwards, I. A. (1940) *Amer. Heart J.*, **19**, 338.

Sears, J. B., and Cohen, S. S. (1940) *Surg. Gynec. Obstet.*, **70**, 842.

Stalker, L. K., and Heyerdale, W. W. (1940) *Proc. Mayo Clin.*, **15**, 350.

Varicose Ulcer

Vitamin-B₁ Therapy

A. Ochsner and M. C. Smith treated 10 patients suffering from painful varicose ulcers with vitamin B₁. Vitamin B₁ had previously been used with success by other observers in the treatment of chronic painful lesions including varicose ulcers. In this series the patients were relieved of their symptoms in an average of 5 days. In 8 of the patients the pain was completely relieved. A diet high in vitamin B₁ and a daily dose of aneurine up to 30 mg. were given. It is probably better, as in the treatment of neuritis, to give large daily doses until relief is obtained rather than small doses over a long period. How vitamin B₁ affects the pain is not known, unless it supplies a deficiency due to poor intake or diminished absorption.

Histamine Iontophoresis

S. V. Gould-Hurst states that varicose ulcers which have failed to respond to other recognized methods can be successfully treated by histamine iontophoresis, assisted in some cases by the application of ultra-violet light to the ulcer and surrounding skin. A ring of skin surrounding the ulcer, $\frac{1}{2}$ inch wide, is cleaned with alcohol. A thin layer of ointment containing 2 per cent of histamine acid phosphate is spread over half of this area of skin, care being taken not to allow any ointment to touch the raw surface of the ulcer. A pad of gauze soaked in warm saline solution is then placed over the anointed area. The positive terminal of a galvanic battery is bound on to this pad, and the negative electrode is applied to

some convenient adjacent area. A constant current of 4 to 6 ma is slowly turned on, and allowed to pass either for 5 minutes or until the patient complains of headache or other discomfort. At the next treatment the other half of the surrounding skin area is treated. At subsequent sittings both the amount of current passed and the time of treatment are increased, but never pushed beyond the point of moderate headache. A current of 10 ma for 12 minutes is about the average application that can be received with only the mildest discomfort. After each treatment the patient should rest for 15 minutes. A dressing of sterile soft paraffin or of cod-liver oil is applied, and the wound covered with gauze and firmly bound over a thin layer of wool. After two or three such treatments the edge of the skin round the ulcer takes on a fresh pink appearance, and the ulcer begins to heal from without inwards. A mild erythema dose of ultra-violet light, once a week, to the affected limb appears to speed up healing, and leave a more supple scar.

Gould-Hurst, S. V. (1940) *Lancet*, **1**, 739

Ochsner, A., and Smith, M. C. (1940) *J Amer med Ass.*, **114**, 947.

Phlebitis

Treatment

Novocain infiltration of lumbar sympathetic.—J. Marmasse treated a case of bilateral phlebitis following labour by means of infiltration of the lumbar sympathetic with novocain. The left lumbar sympathetic was infiltrated with 20 c.cm. of a 1 per cent solution of novocain. There was a sensation of warmth immediately experienced. The leg was immobilized and the foot of the bed raised on blocks. Pain quickly disappeared. On the third day pain was felt in the right leg, and the right lumbar sympathetic was infiltrated. On the fourth day the left sympathetic was again infiltrated. The patient was able to get up on the 24th day.

Marmasse, J. (1940) *Bull. Soc. Gynéc. Obstet.*, **28**, 521.

Thrombosis

Prevention

Heparin.—G. Murray has used purified heparin both experimentally and clinically to prevent thrombosis after surgical operations on blood vessels. Heparin is a strong organic acid, probably mucotrin trisulphuric acid. The crystalline barium salt can be given without producing toxic effects. An intravenous dose raises the clotting time, which can be maintained by repeated doses at any desired level. When a single vessel is operated on it may be injected just proximal to the area of repair, thus increasing the clotting time there without affecting the rest of the circulation. The injections were used effectively to prevent thrombosis in many cases of venous grafts and anastomoses of vessels. Blood transfusions can be given with its aid, without the danger of clotting. There was no thrombosis or embolism in 400 hospital patients treated with heparin. Thrombophlebitis was benefited by this means. Twenty-nine patients with pulmonary embolism were treated with heparin. None of the patients died, and except for one case had no further emboli. Twelve cases were successfully treated by embolectomy. Murray stressed the importance of this substance in the prevention as well as cure of thromboses and embolism.

Murray, G. (1940) *Arch. Surg., Chicago*, **40**, 307

Thrombophlebitis

Treatment

Elastic adhesive bandages in prevention of embolism.—W. Leun reports excellent results in the prevention of embolism in thrombophlebitis from the application of pressure by elastic adhesive bandages. The technique is as follows. The leg is shaved and a tightly twisted wad of cotton-wool about 6 cm. long and 3 cm. in diameter, is dusted with powder and placed transversely and under pressure over the femoral vein. The entire leg is then bandaged with elastoplast, beginning at the toes. The foot should be in a position between 90° and 100° to prevent the bandage from pressing the ankle when walking. It is important that the skin and

bandage should not form wrinkles; the bandage should not be applied while the leg is swollen, and should remain in position until all danger of embolism is past, generally about 4 weeks.

Procaine hydrochloride injection—A Ochsner and M. DeBakey stated that thrombophlebitis is probably produced by spasm of the arterial and venous systems in the part. The exchange of fluids around and within the vessels is therefore upset. The authors blocked these impulses by injecting procaine hydrochloride into the sympathetic ganglia. In 15 patients so treated the pain was promptly relieved. The temperature dropped, the oedema disappeared and 60 per cent of the patients were cured within 8 days of the treatment.

Leun, W. (1939) *Munch. med. Wschr.*, **86**, 1271.

Ochsner, A., and DeBakey, M. (1940) *J. Amer. med. Ass.*, **114**, 117.

VERTIGO

See also B.L.M.P., Vol. XII, p. 544; and Surveys and Abstracts 1939, p. 593

Clinical Picture

B. H. Shuster discusses the clinical aspects of vertigo; it may be described as a sensation of giddiness, rotation, or pulsion, occurring in attacks and not constantly present. As equilibrium depends upon superficial and deep skin and muscle sensation, visual impressions and vestibular responses, disorders of these or of the conducting tracts or central nuclei, may produce vertigo. In every case, a complete general, neurological, and vestibular examination is called for, including rotation tests and caloric tests. External ear disease and middle-ear disease must be excluded. Sudden onset of vertigo should suggest suppurative labyrinthitis or labyrinthine haemorrhage. For cases of vertigo for which a cause cannot be discovered reduction in salt and fluid intake is advised, together with large doses of ammonium chloride (45 gr. three times a day). In expert hands, division of the vestibular portion of the 8th nerve gives good results.

Shuster, B. H. (1939) *Arch. Otolaryng., Chicago*, **30**, 536.

Labyrinthine or Aural Vertigo

Treatment

Portmann's operation—E. M. Woodman stated that labyrinthine vertigo appears to be due to labyrinthine hypertension. Blockage of the Eustachian tube may lead to this condition and it is then usually cured if the tube is dilated with bougies. Labyrinthine vertigo rarely calls for operation, but, when it does, Portmann's operation is often successful. This consists of opening the ductus vestibuli through the petrous bone. The operation should never be done if middle-ear sepsis is present. In a series of 11 cases, vertigo was cured in 8, tinnitus was cured in 2 and greatly improved in 1; hearing was practically restored to 1 case, in 5 it was improved, 1 was made worse, and 4 were unaffected. There were no fatalities in this series.

Labyrinthectomy—M. Yearsley records a further case of deliberate destruction of the semicircular canals for incurable severe labyrinthine vertigo, with a successful result. The operation was performed in 1938 under avertin and ether anaesthesia. The right auricle was turned down, the antrum was widely opened, and the tympanic membrane and major ossicles were removed. The ampulla of the external semicircular canal was opened and followed into the vestibule, and the ampullae thereof and of the superior and posterior canals were curetted. The vestibule was swabbed with a 2 per cent solution of formaldehyde. Finally the cavity was packed and the auricle readjusted, the lower part of the original incision being left open for the packing of the lateral sinus. This was the sixth successful case of labyrinthectomy performed by the author since 1908.

Woodman, E. M. (1939) *Proc. R. Soc. Med.*, **32**, 1642.

Yearsley, M. (1940) *Lancet*, **1**, 548.

Ménière's Syndrome*Treatment*

Ammonium chloride and potassium nitrate—M. N. Walsh and A. W. Adson discussed the merits of medical and surgical treatment of Ménière's syndrome. The condition may be treated medically with a low-sodium diet combined with the ingestion of ammonium chloride in a dosage of 9 g. daily for 3 days, then taking the low-salt diet alone for 2, and continuing in this manner. Potassium nitrate in a dosage of 9 g. daily for 3 days, then discontinued for 2 days, may be used instead of the chloride since it does not produce gastro-intestinal disturbances. Elimination of septic foci combined with sedation may be used. On the whole those with unilateral deafness do better on medical treatment than those in whom it is bilateral.

Surgical—Walsh and Adson said that, if medical treatment fails, section of the vestibular part of the eighth cranial nerve gives good results. Surgical intervention is indicated if the vertigo interferes with the patient's occupation or if he cannot afford the time to be constantly coming to hospital for medical treatment.

High potassium intake—J. H. Talbott and Madeline R. Brown investigated the aetiology and treatment of Ménière's syndrome. In 48 cases the concentrations of the acid-base constituents of the serum were determined. There was no constant variation in any of them except that during an attack 4 patients showed an increased concentration of serum potassium and a decreased concentration of serum sodium. By giving large amounts of sodium salts intravenously and orally an attempt was made to induce an attack in 4 patients, but it was unsuccessful. The authors have treated many patients with a diet of normal sodium content supplemented by a high potassium intake, the latter was effected by giving 6 to 10 g. of potassium chloride daily in an aqueous solution which produced some clinical improvement although it did not prevent the attacks.

Histamine by intravenous injection—C. H. Shelden and B. T. Horton report the successful treatment of the acute symptoms of Ménière's syndrome by the intravenous injection of 1.9 mg. of histamine acid phosphate dissolved in 250 c.c. of physiological saline. The injection is given slowly and occupies 1½ hours. No bad effects were produced, and most of the patients had previously received Furstenberg's treatment, ammonium chloride and a low salt diet, without benefit. Fifteen patients were given histamine, the first 4 were injected hypodermically and the 11 others intravenously, the latter all responding in a spectacular manner, and not having any other treatment. Horton in 1927 used histamine to relieve hypersensitivity to cold, and with Maclean and Craig (1939) in 'a new syndrome of vascular headache', or 'erythromelalgia of the head', one patient with this new syndrome was also relieved from the symptoms of Ménière's syndrome, and hence the treatment was initiated. Shelden and Horton consider it probable that the cause of Ménière's syndrome is a local alteration in the permeability of the capillary wall in the labyrinth with secondary oedema. H. W. Woltman pointed out that in the differential diagnosis of acoustic nerve tumours from Ménière's syndrome, the vertigo is rarely so severe as in Ménière's syndrome, and that diminution of the corneal reflex on the side of the tumour is a prominent sign in the tumour case.

Dietary rich in vitamins—J. Adam reported a case of Ménièreism and migraine which was greatly relieved, if not cured, chiefly by dietetic treatment. The woman, aged 40, had in 1933 violent sickness, vomiting, and giddiness, accompanied by deafness and hissing tinnitus in the right ear. Several attacks of this nature occurred until, in 1939, she was laid up for several weeks with severe giddiness. Right-sided migraine began in 1939. Under treatment consisting in a dietary rich in vitamins, particularly vitamin C—a blue pill, once a week, and a mixture containing trinitrin, gelsemium, strychnine, and bromide she had been free from migraine and giddiness for a period of 6 months.

Adam, J. (1940) *J. Laryng.*, **55**, 224.

Horton, B. T. (1927) *Proc. Mayo Clin.*, **2**, 276.

— Maclean, A. R., and Craig, W. McK. (1939) *ibid.*, **14**, 257.

Shelden, C. H., and Horton, B. T. (1940) *Proc. Mayo Clin.*, **15**, 17.

Talbott, J. H., and Brown, M. R. (1940) *J. Amer. med. Ass.*, **114**, 125.

Walsh, M. N., and Adson, A. W. (1940) *J. Amer. med. Ass.*, **114**, 130.

Woltman, H. W. (1940) *Proc. Mayo Clin.*, **15**, 20.

VITAMINS

See also B.E. M. P., Vol. XII, p. 570; Cumulative Supplement, Key Nos. 1601-1609; Surveys and Abstracts 1939, p. 594; and pp. 16, 31, 56, 70, 114, and 117 of this volume.

Vitamin A*Physiology*

Vitamin-A blood level.—C. D. May *et al.* stated that the level of vitamin A in the blood appears to be a useful direct clinical test for early diagnosis of deficiency of vitamin A. In infants and children deficiency of vitamin A may be detected by a low level of vitamin A in the blood before other reliable clinical signs appear.

Effect of depletion diet on blood values.—G. Steininger *et al.* investigated the vitamin-A levels in 5 normal adults over periods of from 2 to 4 months. During this time 4 of the subjects lived on a vitamin-A deficient diet except for two short periods of supplementation. The vitamin A and blood carotene levels of 34 other adults were also determined once to obtain a normal range of values. Half of these subjects had received a supplement of vitamin A. The results showed that the amount of vitamin A in the blood depended upon the amount in the diet. Biophotometer readings show no correlation with the level of the blood vitamin A. The blood level determination is only of value in showing whether the intake is high or whether it is low enough to deplete the body's store of the vitamin.

Hypovitaminosis A

Dark-adaptation test.—I. J. Harris and M. A. Abbasy assessed the value of the dark-adaptation test as a test for vitamin-A deficiency. The tests were made with a modified Birch-Hirschfeld photometer and were made on various cross-sections of the population. The subjects were repeatedly retested to check the reliability of the result and those found below normal were divided into 2 groups, one group receiving adequate quantities of vitamin A and the other group acting as controls. The readings were rarely low in middle-class adults and treatment with vitamin A did not improve them beyond normal. The children who were found subnormal returned to normal after treatment, whereas the control group who received no vitamin A did not. Dark-adaptation tests in various social classes among children showed that the result could be correlated with the diet, a diet low in vitamin A producing a subnormal result. Harris and Abbasy stated that the test is only of value for detecting vitamin-A deficiency and cannot be used for quantitative assessment. It is only applicable to experimental groups, since the apparatus is too complicated to be used by the general practitioner.

Effect of Liquid Paraffin on Absorption

A. C. Curtis and R. S. Ballmer investigated the effect of liquid paraffin on the absorption of carotene. The blood carotene level was taken as the index of absorption. It was found that liquid paraffin, emulsions of liquid paraffin, and emulsions of liquid paraffin with agar, taken in amounts of 20 c.c. 3 times a day before meals, or twice a day before the morning and evening meals, interfered with the absorption of carotene. If the liquid paraffin were saturated with carotene at room temperature it still interfered with the absorption of carotene from food in the intestine. If it were saturated at body temperature the absorption of carotene was not interfered with. If emulsified forms of liquid paraffin were used, comparable results were obtained.

Curtis, A. C., and Ballmer, R. S. (1939) *J. Amer. med. Ass.*, **113**, 1785.

Harris, I. J., and Abbasy, M. A. (1939) *Lancet*, **2**, 1299, 1355.

May, C. D., Blackfan, K. D., McCreary, J. F., and Allen, F. H. (1940) *Amer. J. Dis. Child.*, **59**, 1167.

Steininger, G., Roberts, L. J., and Brenner, S. (1939) *J. Amer. med. Ass.*, **113**, 2381.

Vitamin B₁*Urinary Excretion and its Significance*

F. Sciclounoff discusses the question whether or not the determination of the vitamin-B₁ content of the urine is of any clinical value. The amount of B₁ excreted daily is given by various authors as between 30 and 500 µg. The author found in healthy persons from 30 to 200 µg. per day. In some seemingly healthy persons there was not any B₁ in the urine. If additional vitamin B₁ is given by mouth, from 5 to 35 per cent of this extra intake is excreted; other authors found only 3 to 5 per cent. If aneurine is given parenterally, from 15 to 38 per cent of the extra intake is excreted; taking into consideration other authors' findings, the average excretion of aneurine given parenterally seems to be 25 per cent.

In cases of gastric ulcer, atrophic hepatic cirrhosis, and Addison's disease, the excretion amounted to 5 per cent only of the intake. It could not, however, be proved that this reduced excretion was due to an increased want or to an insufficiency of excretion. In cases of avitaminosis B₁ there is no aneurine in the urine, even after large doses of aneurine. In some cases of beri-beri there is a large excretion after injection. Absence of aneurine in the urine does not always prove that there is lack of it. Some of the factors influencing the excretion of aneurine are the destruction of the substance in the tissues (about 75 per cent), alkalosis of the body fluids, alcohol, and other unknown causes.

The author concludes that the amount of vitamin B₁ excreted with the urine is not of any clinical value.

Hypovitaminosis B₁ and Cardiac Insufficiency

I. Langeron discusses the myocardium in chronic alcoholism and avitaminosis B₁ and describes the chemical and anatomical features of alcoholic myocardial failure (large liver, dyspepsia, polyneuritis, cardiovascular insufficiency with dyspnoea, tachycardia, oedema) with the typical repeated attacks of insufficiency eventually resulting in death. There is no anatomical finding which explains the cardiac symptoms. The heart of the beri-beri patient shows very similar signs (Wenckebach) and in 1933 Campbell and Allison found that there probably exists a 'beri-beri nostras' with a predominance of cardiac symptoms. This 'beri-beri nostras' might be caused either by a reduced intake of vitamin B₁ (due to wrong diet) or poor utilization due to infections, toxic states, or hepato-gastric disorders. The clinical characteristics of Asiatic beri-beri are polyneuritis, dyspnoea, tachycardia, cardiac instability, oedema disproportionate to the changes in the heart, dilatation of the heart, arterial hypertension, and enlarged liver. The aetiological conditions of alcoholic myocarditis are similar to those of 'beri-beri nostras'. It is mostly young and manual workers who are affected with insufficient nourishment or with gastric trouble. There is also a similarity in the electro-cardiograms.

A case already published (1937) is described in which alcoholic myocarditis was treated with vitamin B₁ with excellent results (diuresis, disappearance of oedema and polyneuritic symptoms). The author concludes that there is a 'beri-beri nostras' and that alcoholic myocarditis is in its pathogenic condition similar to avitaminosis B₁ or 'beri-beri nostras'.

Therapeutic Applications

Intraspinal injection in degenerative nervous diseases—T. R. Robie employed intraspinal injections of vitamin B₁ in 19 cases of chronic degenerative nervous diseases and in one case of alcoholic polyneuritis. Severe reactions often followed these injections. In the chronic degenerative nervous disorders no sustained improvement occurred. The case of alcoholic polyneuritis was cured by the intramuscular injection of vitamin B₁. The lack of improvement in these cases indicated that hypovitaminosis B₁ is not the basic cause of the degenerative disorders, and probably not even an important factor in their development or rate of progress.

Neuritis of eighth cranial nerve—K. C. Brandenburg stated that the underlying cause of all neuropathies, whether due to diabetes, toxins, pregnancy, etc., is probably a deficiency of vitamin B₁. The ordinary diet is not very high in vitamin B and the liver stores are quickly depleted. Loss of hearing, nystagmus, and visual symptoms often occur in other diseases due to vitamin-B deficiency. The author

reported a case of bilateral deafness and tinnitus following irradiation for carcinoma of the cervix which was cured by 10 and 15 mg. of aneurine chloride given intravenously for 9 days. He suggested that this treatment, combined with a diet adequate in vitamin B, might be used in other cranial nerve neuropathies.

Brandenburg, K. C. (1940) *Arch. Otolaryng., Chicago*, **31**, 189.

Langeron, L. (1937) *Arch. Mal. Cereu.*, **30**, 609.

— (1939) *Pr. méd.*, **47**, 1189.

Robie, T. R. (1940) *Amer. J. Surg.*, **48**, 398.

Seiclouhoff, I. (1939) *Schweiz. med. Wschr.*, **69**, 665.

Vitamin-B₂ Complex

Ariboflavinosis

Ocular manifestations—V. P. Sydenstricker *et al.* cured 47 patients with ocular symptoms and signs of ariboflavinosis by the administration of riboflavin. The most frequent symptoms were photophobia and dimness of vision not corrected by adjustment of refractive errors. Burning sensations in the eyeballs, 'roughness' of the eyelids, and extreme visual fatigue were almost equally common. Nine patients showed marked impairment of visual acuity in the absence of refractive errors or opacity of the media. The earliest and most common sign was circumcorneal injection; this was present in 45 cases; it was often grossly visible, it could frequently be seen with a hand lens or ophthalmoscope, and it was always obvious on slit-lamp inspection as marked congestion and proliferation of the limbal plexus. In cases not showing limbal congestion, arcus senilis and cataract were present. Gross injection of the vessels of the fornix and sclera without evidence of infection was seen in all but 4 of the cases with corneal congestion. In 37 cases there was actual invasion of the cornea by capillaries from the limbal plexus. Superficial nebulæ of the cornea were present in 18 cases, and superficial punctate opacities in 2. Interstitial nebulæ were relatively uncommon. These manifestations cleared up on the administration of 5 to 25 mg. of riboflavin daily.

Sydenstricker, V. P., Sebrell, W. H., Cleckley, H. M., and Kruse, H. D. (1940) *J. Amer. med. Ass.*, **114**, 2437.

Vitamin C

Physiology

Properties. E. Wille found that vitamin C increases the blood sugar during hypoglycaemic fits and that it prevents fits when given persistently. When insulin shock is induced in schizophrenics, vitamin C raises the blood-sugar level; patients wake up much more quickly when vitamin C is given before the sugar. There is a connexion between vitamin C and carbohydrate metabolism. In view of the effect of vitamin C on diseases affecting the metabolism of muscle glycogen, and of its effects on schizophrenics, it appears probable that vitamin C is necessary for carbohydrate metabolism as a 'redox potential' producer.

Influence of ascorbic acid on hepatic function, and relation to vitamin B₁ - O. Murakami of the second Medical Clinic of Kyoto University has reported the results of his experimental investigations on the influence of ascorbic acid upon the liver function and the mutual relation between vitamins B₁ and C. The liver and the adrenal cortex are the richest in the body in vitamin C and the liver is the most important organ in connexion with metabolism, and it is therefore probable that a certain relation exists between hepatic function and the amount of vitamin C in the liver. His results are published in six reports. In the first report on the influence of ascorbic acid upon the pigment-excreting function of the liver it is shown that in guinea-pigs fed on a diet deficient in vitamin C for some time the amount of bile and the pigment-excreting function of the liver are diminished in correspondence with the smaller amount of vitamin C in the liver. Subcutaneous injection of *l*- or *d*-ascorbic acid into the guinea-pigs with C-hypovitaminosis corrects the disturbance of hepatic function and raises a low vitamin C content of the liver. The effect of *l*-ascorbic acid is a little stronger than that of *d*-ascorbic acid, and repeated small doses of ascorbic acid are more powerful than a single large dose. In report 2, on the influence of ascorbic acid on the sodium santonium-control

of the liver, evidence is given that this detoxicating function of the liver rises, falls and runs parallel with the amount of ascorbic acid in the liver. In report 3 the same relation is shown to exist between the amount of ascorbic acid in the liver and that organ's power of detoxicating indole. Report 4 deals with the mutual relationship between vitamins B₁ and C in regard to the indole detoxicating function of the liver of guinea-pigs with C-hypovitaminosis, especially the influence of vitamin B₁ upon the effect of vitamin C in detoxication. It was found that the injection for 3 days of 10 mg. of *l*- or *d*-ascorbic acid into guinea-pigs with C-hypovitaminosis increased the indole-detoxicating power of the liver, whereas similar injections of 0.1 mg. vitamin B₁ did not have this effect. But the effect of injection of both these vitamins together was much greater than the sum of the two separate injections of the 2 vitamins; thus the addition of a small quantity of vitamin B₁ markedly increased the effect of ascorbic acid. Report 5 shows that injection of ascorbic acid into the central artery of the rabbit's ear causes temporary dilatation of the peripheral vessels. In report 6 it was shown that similar injection of vitamin B₁ produced slight contraction of the peripheral vessels, but that the addition of a small quantity of vitamin B₁ to a low concentration of a solution of *l*- or *d*-ascorbic acid and similarly injected into rabbits markedly increased the dilatation of the peripheral blood vessels.

Hypervitaminosis C

H. Rietschel states that most authors do not recognize a hypervitaminosis due to vitamin C. He found that infants given large doses of vitamin C showed an increase in the number of thrombocytes in the blood. Some of the children also became restless and had diarrhoea. In adults the symptoms were similar. The author took on each of five consecutive days 500 mg. of vitamin C and found an increase in the number of thrombocytes in his blood; he also suffered from sleeplessness and diarrhoea. The symptoms disappeared directly he discontinued the vitamin C. There is no danger of hypervitaminosis due to vitamin C in ordinary food. It may, however, occur among vitamin fanatics and in hospitals where vitamin C is given for therapeutic purposes. The danger is very small as vitamin C is easily oxidized, and large amounts are required in persons suffering from infective diseases, in pregnant women, and after muscular exercise. Hypervitaminosis due to vitamin C is likely to appear when vitamin C is given over long periods in quantities of 200 to 500 mg. daily.

J. D. Croft and L. D. Snorf investigated the blood ascorbic acid concentration in 100 unselected patients. In 38 the concentration was found to be below normal. Although the levels were as low in some cases as in scurvy, no cases of scurvy were seen. Oral sepsis and dental caries were, however, far more common in the deficient group than in the others. This deficient group also showed a high percentage (84 per cent) of dysfunction or disease of the gastro-intestinal tract. Forty per cent had active peptic ulcers. No correlation was found between anaemia and low ascorbic acid concentration in the blood. Six patients with low acid plasma levels and anaemia were given 75 to 100 mg. of synthetic ascorbic acid daily by mouth but no reticulocyte response occurred. There were very low vitamin C blood levels in several cases with no clinical manifestations.

Therapeutic Applications

Hypovitaminosis as cause of intestinal disease—F. M. Woolsey and J. R. Black, investigating 24 cases of intestinal disease of varied types, found on microscopical examination of the lesions at necropsy that 12 of these showed fusiform bacilli. All of these 12 patients had been on diets deficient in vitamin C, and all but 2 had infections which could cause breaks in the mucosa. Of 21 guinea-pigs fed on a diet deficient in vitamin C and also given fuso-spirochaetes, 1 acquired an intestinal lesion, while none of the control animals showed such a lesion. The authors suggested that fuso-spirochaetes could gain a foothold in the intestine when there was a break in the mucosa, and that such breaks occurred as a result of haemorrhage in the mucosa from vitamin-C deficiency, as well as through the activity of bacteria and protozoa.

In skin diseases—W. F. Lever and J. H. Talbott investigated the vitamin-C content of the blood in 61 apparently healthy persons, and in 181 patients with

various skin diseases. They concluded that there is no direct relation between the vitamin-C content of the blood and the development of the skin diseases which were investigated. It was found that most patients with pemphigus, purpura, or generalized exfoliative dermatitis had low levels of vitamin C in the blood. In other diseases there was a wide variety of values. Five patients with urticaria, 2 with psoriasis, 1 with purpura, and 1 with pemphigus were treated with 200 mg. vitamin C daily for periods of from 2 to 10 weeks. None of these patients showed improvement attributable to the high vitamin-C intake.

In surgical patients.—J. A. Wolfer and F. C. Hoebel investigated the significance of ascorbic (cevitamic) acid deficiency in surgical patients. They concluded that, although at present there is no absolute proof of the relation of vitamin-C deficiency to non-union of wounds in human subjects, there is considerable evidence, historical, pathological, experimental, and clinical, to give strong support to the existence of such a relationship. If the blood ascorbic acid is low and there is a history of deficient or defective intake of vitamin-C-containing foods, the patient may be considered to have a tissue depletion. Patients deficient in vitamin C may be saturated by large doses of ascorbic acid given by mouth or intravenously (1 g. of ascorbic acid for a period of 10 days, then about 0.3 to 0.5 g. daily until the wound is healed) or by a dietary adequate in vitamin C. Vitamin-C deficiency should be considered as possibly present in patients taking large doses of alkalis by mouth, those with obstructive gastro-intestinal lesions, particularly at or above the pylorus, those with a history of vomiting over long periods, those with hypermotility of the small intestine, and in syphilitics and alcoholics. After operation normal patients may show a drop to scurvy levels because of long periods of intravenous therapy without food by mouth, because of abnormal bowel physiology, and because of the increased utilization of vitamin C that apparently accompanies infections and operative procedures.

Croft, J. D., and Snott, I. D. (1939) *Amer. J. med. Sci.*, **198**, 403.

Lever, W. F., and Talbott, J. H. (1940) *Arch. Derm. Syph.*, N.Y., **41**, 657.

Murakami, O. (1939) *Japan. J. Gastroenterol.*, **11**, 1-48.

Rietschel, H. (1939) *Klin. Wschr.*, **18**, 923.

Wille, L. (1939) *Deutsch. med. Wschr.*, **65**, 1117.

Wolfer, J. A., and Hoebel, F. C. (1939) *Surg. Gynec. Obstet.*, **69**, 745.

Woolsey, L. M., and Black, J. R. (1939) *Arch. Path.*, **28**, 503.

Vitamin-D Complex

Therapeutic Applications

Vitamins D₂ and D₃ in osteomalacia and late rickets.—D. C. Wilson compared the relative potency of vitamins D₂ and D₃ in the treatment of osteomalacia and of late rickets. Thirteen pairs of patients with osteomalacia and 2 pairs with late rickets received one or other drug. The vitamin D₂ was given as irradiated ergosterol and D₃ as irradiated 7-dehydrocholesterol. A weekly dose of 21,000 I U. of either substance had good and equal results. Pain, carpopedal spasm, and difficulty in walking disappeared in successful cases.

Comparative effects of vitamins D₂ and D₃ in infantile rickets.—N. Morris and M. M. Stevenson compared the therapeutic efficiency of vitamins D₂ and D₃ in 12 children with infantile rickets. To 6 of these children vitamin D₂ was given and to 6 vitamin D₃, in amounts equivalent to 2,000 I U. daily. The disease was active in these patients and the rate of healing was measured by X-ray examination of the wrists and estimation of the plasma phosphatase. No difference in the rate of healing or progress of the disease in the two groups was found.

Morris, N., and Stevenson, M. M. (1939) *Lancet*, **2**, 876.

Wilson, D. C. (1940) *Lancet*, **1**, 961.

Vitamin D and A.T.10

Therapeutic Applications

In thyroid and parathyroid deficiency.—H. P. Himsforth and M. Maizels assessed the value of vitamins D₂ and D₃, and A.T.10 (dihydrotachysterol) in the treatment

of congenital thyroid and parathyroid deficiencies. The patient was a mentally and physically retarded boy of 13 years who suffered from epileptic fits. He also had bilateral cataracts and tetany. His basal metabolic rate was -25 per cent and his serum calcium 5 mg per 100 c.c. He received thyroid $1\frac{1}{2}$ gr. daily and the basal metabolic rate rose to $+10$ per cent. Now, 6 years later, the boy appears healthy and can do simple work in a shop. In spite of treatment for parathyroid deficiency tetany sometimes occurs. The cataracts were successfully removed by operation. The parathyroid deficiency could be controlled by oral dosage of vitamin D_2 (calciferol) in oil, 500,000 units weekly. After years of this treatment there have been no ill-effects, despite the large dosage used. Vitamin D_3 gave as good results, as also did A T 10, though this preparation was not so reliable in its actions. The two deficiencies did not depend upon each other, treatment for the hypothyroidism had no effect upon the tetany and *vice versa*.

Himsworth, H. P., and Maizels, M. (1940) *Lancet*, **1**, 959

Vitamin K

Properties of Phthiocol

S. Vukov reviewed knowledge on vitamin K and the role of phthiocol in exerting its anti-haemorrhagic activity. Phthiocol (2-methyl-1, 4-naphthoquinone), a simple chemical substance, possesses as much anti-haemorrhagic activity as a more complex vitamin-K compound. It has been employed intravenously in cases of hypoprothrombinaemia, and a definite rise in the prothrombin level has been obtained in practically all cases, the response occurring in less than $1\frac{1}{2}$ hours. The reaction by which prothrombin is increased after phthiocol administration occurs within the liver cell. The use of bile for vitamin-K absorption from the gastro-intestinal tract is simply mechanical in that it aids emulsification, solution, and absorption of fats. Given intravenously, no bile is necessary. The author suggests that perhaps the quinone structure is in some way associated with the prothrombin molecule. The toxicity of phthiocol is minimal. It is particularly valuable in cases of emergency, as in post-operative bleeding, and in cases in which the oral use is impossible or impracticable.

Synthetic Substances with Properties of Vitamin K

Naphthoquinone derivatives—H. R. Butt *et al.* pointed out that vitamin K has been isolated and synthesized and that several other derivatives of naphthoquinone have been proved to have marked anti-haemorrhagic properties. They investigated this property in several of these substances. 1:4-dehydroxy-2-methyl-3-naphthaldehyde given intravenously lowered the prothrombin clotting time of 8 out of 10 patients. The other 2 suffered from cirrhotic livers and damaged liver function. 2-methyl-1, 4-naphthoquinone was also given. It has been found by other workers to have the most marked anti-haemorrhagic activity. Given both orally and intravenously to 20 patients it was found to be effective though it also failed in the presence of liver damage.

Vitamin-K Activity of Naphthohydroquinone Derivatives

I. M. Hellman *et al.* studied the vitamin-K activity of various naphthohydroquinone derivatives in the newly-born infant. They found that, in small unit-equivalent doses, 2-methyl-1, 4-naphthoquinone, 2-methyl-1, 4-naphthohydroquinone dipropionate, and 2-methyl-3-phytyl-1:4-naphthoquinone, dissolved in oil, were capable of raising the plasma prothrombin of the newly-born infant, when given by mouth to the mother during labour. In similar doses, intravenously, 2-methyl-1, 4-naphthohydroquinone-3-sodium sulphionate was shown to possess significant vitamin-K activity. On the other hand, under identical conditions, 2-methyl-1, 4-naphthohydroquinone in milk-sugar pills, and vitamin-K concentrate, by mouth, and 2-methyl-1, 4-naphthohydroquinone-3-sodium sulphionate, intramuscularly, was not found to be effective in raising the plasma prothrombin levels of newly-born infants.

Effect on Prothrombin Blood-Levels

J. D. Stewart and G. Margaret Rourke investigated the prothrombin blood-level

in man and its relation to vitamin K. They found that the prothrombin level normally remains almost stationary. In obstructive jaundice it is very much reduced and a vitamin K and cholic-acid mixture taken by mouth quickly restores it to normal. The prothrombin level may be reduced in such conditions as chronic infection, cirrhosis of the liver, malnutrition and cachexia when vitamin-K therapy may be of value. In haemorrhagic conditions such as haemophilia and purpura the prothrombin blood-level is not reduced and vitamin-K therapy is of no use.

Hypovitaminosis K

In newly-born.—H. Dam *et al.* (1939, a) consider that a hypovitaminosis K, which is generally moderate, occurs in normal children in the first few days after birth and usually disappears about a week later. From this avitaminosis result a hypoprothrombinaemia which is the cause of the slight haemorrhagic diathesis common in the newly-born infant. The authors established the presence of considerable hypoprothrombinaemia in several cases of icterus gravis of the newly-born, anaemia of the newly-born, and congenital dropsy. In 2 of these cases the administration of vitamin K was followed by a rapid rise in the prothrombin level.

Deficiency in normal and sick infants—H. Dam *et al.* (1939, b) investigated vitamin-K deficiency in normal and sick infants. The sick infants suffered from icterus gravis neonatorum, anaemia neonatorum, or congenital dropsy. In the control group of normal infants some had icterus neonatorum. In this group it was found that hypoprothrombinaemia appears a few days after birth and disappears within a week. This condition is due to lack of vitamin K, probably caused by an insufficient supply in the intestines. Vitamin K is present in only small amounts in milk and the balance is supplied by bacterial activity. It is probable that there is not enough bacterial activity in the new-born infant to supply sufficient vitamin K. This period of hypoprothrombinaemia in the normal infant coincides with the period when a slight haemorrhagic diathesis occurs. It therefore appears that they are due to a lack of vitamin K.

In 6 of 7 sick infants the hypoprothrombinaemia was very marked, in one case it was almost zero. In these very low levels it is probable that some other factor than deficient absorption from the intestine is operating. Examination of the stools showed the bile-ducts to be patent in these cases. Vitamin K, together with bile-salt, was given to one patient and the prothrombin level rapidly increased.

In adults—R. Kark and E. L. Iozner reported 4 cases of vitamin-K deficiency occurring in patients who had received insufficient diets. Three of them also suffered from scurvy and the fourth from pellagra and subclinical scurvy. The prothrombin-time was prolonged in all cases. Since 3 of the patients suffered from syphilis it was also estimated in tertiary syphilitics in a good state of nutrition. It was found to be normal in these controls. The patients were treated with rest, an adequate diet, vitamin C and vitamin K by mouth. The prothrombin-time rapidly returned to normal proving that vitamin-K deficiency can occur in a dietary deficiency in man.

In Haemorrhagic Disease of New-born

I. Newton Kugelmass stated that haemorrhagic disease of the new-born is always due to prothrombin deficiency in the blood. Mild forms of the disease are self-limiting but the severe forms do not respond to any usual form of treatment. They are usually associated with a lowered prothrombin level in the mother during pregnancy. Waddell and du Guerry treated a woman during her fifth pregnancy and she gave birth to a normal child. She had previously had 4 die of haemorrhagic disease. During her sixth pregnancy she refused treatment and her child again died, but treatment during her seventh pregnancy resulted in the survival of her last child. Kugelmass reported 2 cases in which vitamin K given to the infant cured mild haemorrhagic disease of the new-born in 24 hours. It was concluded, however, that the vitamin should not be given if a blood transfusion is available.

Therapeutic Applications

Response to synthetic vitamin K in hypoprothrombinaemia—J. G. Allen and O. C. Julian treated 10 cases of clinical hypoprothrombinaemia with synthetic vitamin K (2-methyl-1,4-naphthoquinone). With each 2 mg. of the drug 0.325 g. of bile salts

was given. Daily prothrombin determinations were made. The total dosage of the drug varied from 24 to 140 mg. In 5 cases the prothrombin rapidly returned to normal. In these cases the condition had been induced by the absence of bile in the intestine, leading to the non-absorption of vitamin K. The response was slower in a case of non-tropical sprue, and there was no response at all in 2 advanced cases of hepatic cirrhosis. These results are as good as those obtained with vitamin K, but there is some doubt whether the synthetic substances have as good anti-haemorrhagic properties as the vitamin. There were no toxic reactions to the drug in this series.

- Allen, J. G., and Julian, O. C. (1940) *Arch. Surg., Chicago*, **40**, 912.
 Butt, H. R., Snell, A. M., Osterberg, A. L., and Bollman, J. L. (1940) *Proc. Mayo Clin.*, **15**, 69.
 Dani, H., Tage-Hansen, F., and Plum, P. (1939, a) *Ugeskr. Laeg.*, **101**, 896.
 — (1939, b) *Lancet*, **2**, 1157.
 Hellman, L. M., Moore, W. T., and Shettles, L. B. (1940) *Johns Hopk. Hosp. Bull.*, **66**, 379.
 Kark, R., and Lozner, F. I. (1939) *Lancet*, **2**, 1162.
 Kugelmass, I. N. (1940) *Arch. Dis. Childh.*, **15**, 97.
 Stewart, J. D., and Rourke, G. M. (1939) *Lancet*, **2**, 403.
 Vukov, S. (1940) *Northw. Med., Seattle*, **39**, 54.
 Waddel, W. W., and du Guerix, P. (1939) *J. Amer. med. Ass.*, **112**, 2259.

Vitamins A and C

In Blood of Surgical Patients

L. Holman studied 70 patients admitted to hospital for operation, with respect to the vitamin-C blood-content. In 44 per cent of these, values of 0.15 to 0.30 mg. per 100 c.c. were found, indicative of a low vitamin C intake. In 9 patients the values fell below 0.15, indicating that they were on the verge of clinical scurvy. Deficiency of vitamin C is of very great importance in surgical patients since this vitamin is intimately concerned with the synthesis and maintenance of the inter-cellular materials which provide the framework for healing. Thirty-eight patients were studied for the vitamin-A blood-content, of these 10 (26 per cent) showed a marked deficiency, and 9 a supersufficiency of the vitamin. A deficiency of vitamin A is of importance in patients who, following operation, are threatened with infections of epithelial structures such as the salivary glands, bronchi, lungs, and alimentary tract, since the effect of deficiency of the vitamin is to produce metaplastic changes in epithelial structures. Surgical patients should be prepared for operation by several days of an optimal diet, rich in proteins.

Holman, L. (1940) *Surg. Gynec. Obstet.*, **70**, 261.

VULVA AND VAGINA DISEASES

See also B.E.M.P., Vol. XII, p. 606, Surveys and Abstracts 1939, p. 600, and p. 22 of this volume.

Vulva

Imperforate Hymen with Haematocolpos

P. Tompkins reviewed the literature of 113 cases of imperforate hymen with haematocolpos, and reported 5 cases. The obstruction produces dilatation of the vagina, then of the cervix and uterus, and finally of one or both tubes. The dammed-up blood is thick, tarry, and sterile. The three main symptoms of the condition are amenorrhoea, lower-abdominal pain, and bladder symptoms such as difficulty in voiding. Complete excision of the hymen followed by a high Fowler position to promote drainage is the operation of choice. There is danger of ascending infection leading to pelvic peritonitis after operation. No examination should be made until two menstrual periods have occurred, and then only with sterile precautions.

Post-Partum Labial and Paravaginal Haematomas

H. G. Hamilton reported 12 cases of post-partum labial or paravaginal haematoma. The haematoma may be immediate or delayed, the first type appearing as soon as the labour is finished. The haematoma spreads rapidly and is accompanied by excruciating pain. The area of dissection of the haemorrhage depends upon whether it occurs above or below the pelvic fascia and levator ani muscles. The condition is not always entirely due to trauma and a haemorrhagic condition during pregnancy may account for it. Successful treatment depends a good deal on early diagnosis. The haematoma should be incised and the clot cleared out. The cavity should be loosely packed and the vagina tightly packed and a T-binder applied. The packing is removed in 12 to 24 hours. A blood transfusion should be given if necessary. This treatment gives very good results. There was one death in this series of 12 cases and that patient had been treated by conservative, expectant treatment.

Infective Granulomas

F. von Haam investigated the macroscopic and microscopic appearances of 155 cases of infective granulomas of the vulva. Of these 104 were venereal, and included cases of syphilis, gonorrhoea, chancroid, venereal lymphogranuloma, and inguinal granuloma; 31 were non-venereal, and included cases of pyogenic granuloma, saprophytic granuloma, fuso-spirochaetal granuloma, and tuberculosis. There were 11 cases of granulomas of mixed aetiology and 9 of unknown aetiology.

Pruritus Vulvae

Magnesium sulphate injections - A. Seimeanu and C. Adamesteanu discuss 51 cases of genuine pruritus vulvae, i.e. cases where they could not find underlying cause for the pruritus. The pruritus manifested itself in attacks of long duration. The age of the patients was from 28 to 68 years. Most of them showed signs of lichenification due to scratching. Local treatment was of little use, but epidural injections of a 20 per cent solution of magnesium sulphate proved to be very successful. The authors are of the opinion that pruritus vulvae is a phenomenon of the sympathetic nervous system. There may be various causes for the hyper-excitation of the autonomic nervous system, either general, such as intoxication or endocrine disorder, or local, such as pressure upon the sacral part of the autonomic nervous system. The biological cause of the pruritus is probably a deprivation of magnesium in the autonomic nervous system. They think that the injection of magnesium sulphate enriches the autonomic nervous system with magnesium and re-establishes the calcium-magnesium equilibrium in the nervous structure.

The authors inject 5 to 6 c.cm. of a pure, sterile and freshly made 20 per cent solution of magnesium sulphate into the epidural space. In very nervous patients they inject 1 to 2 c.cm. of novocain 1 per cent epidurally to prevent pain. The injections are repeated every third day, on an average altogether 4 or 5 times, but as many as 9 are sometimes necessary.

Kraurosis Vulvae

Oestrogenic hormone - E. C. Hamblen concludes that there is little evidence that oestrogenic treatment is of any value, in some patients Goldberger observed temporary relief, but permanent effects were not reported. Vulvectomy seems to be the only certain way of giving any significant symptomatic relief.

Goldberger, M. A. (1933) *Amer. J. Obstet. Gynec.*, **25**, 58.

Haam, E. von (1940) *J. Amer. med. Ass.*, **114**, 291.

Hamblen, E. C. (1939) *Endocrine Gynecology*, p. 425, London.

Hamilton, H. G. (1940) *Amer. J. Obstet. Gynec.*, **39**, 642.

Seimeanu, A., and Adamesteanu, C. (1939) *Pr. méd.*, **47**, 1498.

Tompkins, P. (1939) *J. Amer. med. Ass.*, **113**, 913.

Vagina*Effective Vaginal Cleanser*

Aluminium hydroxide and colloidal kaolin - S. P. Savitz *et al.* stated that most agents used to cleanse the vagina might be objected to because they are ineffective, toxic, or irritating. A mixture of aluminium hydroxide gel, 80 per cent, and colloidal kaolin, 19 per cent, sodium benzoate 0.5 per cent, mixed phenols 0.5 per cent (eucalyptol 1 part, menthol 1½ parts, and thymol 4 parts) was compared with many

common agents such as sodium bicarbonate and silver nitrate. It was found to be very effective. Such a mixture acts by coagulating the mucus and debris which can then be removed by douching with water. A number of cases of non-specific leucorrhoea, leucorrhoea due to mild cervicitis, exocervicitis and endocervicitis and salpingitis were treated successfully by this method. It was employed with good results pretherapeutically for *Trichomonas vaginalis*, and in moniliasis. Half an ounce of the mixture is used with 8 fluid ounces of water. The patient then immediately rinses the vagina with several quarts of warm water. If continued action is desired, the patient should not rinse for several hours after applying the mixture. The pH of the mixture is about 7.0, and it supplies neither acid nor alkali to the vaginal tract. The treatment is harmless and can be repeated as often as desired for salpingitis; 2 fluid ounces of the mixture to 2 quarts of hot water every other day produces good results. The mixture may be employed with good results as a general vaginal cleanser.

Gonococcal Vaginitis

Oestrogenic hormone.—A. Jacoby *et al.* treated 108 female patients suffering from gonococcal vaginitis with oestrogenic hormone in the form of amniotin (oestrone) capsules. Each capsule contained 1,000 I.U., and one capsule was inserted into the vagina every night. Of the patients 85 per cent were apparently cured, but 22 per cent relapsed, thus 63 per cent appeared permanently cured, and 15 per cent were unaffected by the treatment, the vaginal smear remaining positive throughout. The average time for cure was 150 days, and relapses occurred in an average of 109 days later. It is therefore necessary to follow up the cases for a long time to establish a certain cure. There appeared to be no correlation between the vaginal acidity and the presence of positive smears. It was concluded that, although amniotin was a simple and safe method of treatment and appeared beneficial in many cases, its ultimate results were uncertain.

Mycotic Infections During Pregnancy

B. Carter *et al.* discuss the mycoses of the vagina and vulva in 200 cases during pregnancy. That pregnancy disposes to the infection is shown by the presence of yeast-like fungi in 32 per cent of 114 pregnant women and in only 14 per cent of 100 gynaecological patients. Out of the 200 women 86 per cent were infected with fungi belonging to the genera *Monilia*, *Saccharomyces*, or *Cryptococcus*. In 33 per cent of these patients the fungi were found in the vagina, and in 10 per cent on the labia, the vaginal culture being negative. Symptoms such as pruritus only occurred in those infected with the *Monilia*, and trichomonads were often combined with that infection. Five species of *Monilia* were isolated, and trichomonads occurred most often with the Type 3 infection. Skin tests with antigens, and the investigation of the blood for agglutinins were not reliable tests for *Monilia* infection.

Carter, B., Jones, C. P., Ross, R. A., and Thomas, W. L. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 213.

Jacoby, A., Madonia, D. E., Till, S. M., and Wood, T. H. (1939) *Amer. J. Obstet. Gynaec.*, **38**, 140.

Savitz, S. P., Golub, I. J., and Shelanski, H. A. (1940) *Amer. J. Obstet. Gynaec.*, **39**, 329.

WHOOPING-COUGH

See also B.E.M.P., Vol. XII, p. 616; and Surveys and Abstracts 1939, p. 601.

Clinical Picture

Complications

Encephalitis and epilepsy.—C. Worster-Drought reported a case of whooping-cough complicated by encephalitis in a boy aged 5 years which, 5 years later, was followed by epilepsy. When suffering from encephalitis the child had epileptiform attacks. About a year later he became irritable, emotional, and spiteful. No fits occurred and no mental changes were noted. About 4 years later the first fit occurred. A minor attack consisting of twitching of the left eye was noticed. This was repeated, often as many as 3 times in one day. At this time the child was obese and doing moderately well at school work. Up to the present time (5 years later) he has continued to have

fits of varying severity. Sometimes the left side of the face and even the left arm are also involved. He is now mentally backward and rather childish. Treatment with luminal and potassium bromide has kept the fits well in control.

Worster-Drought, C. (1940) *Brit J Child Dis*, **38**, 115

Diagnosis

Skin Test for Susceptibility

L. P. Streat described a skin test for susceptibility to pertussis. In this test an endotoxin is used, and the test bears the same relation to pertussis as the Schick test does to diphtheria. Of the endotoxin, 0.1 c.c. of a 1:600 dilution is used for injection. A patch of erythema measuring 1 to 3 cm. occurs early, or up to 24 hours after injection, in positive cases.

Streat, L. P. (1940) *Canad. med. Ass. J.*, **42**, 525

Treatment

Prophylaxis

Serum therapy. P. Cohen and J. Lapin compare the results of prophylaxis with different vaccines and serums in more than 100 children exposed to whooping-cough infection. A large dose of serum given early in the incubation period was necessary for efficient prophylaxis. Sauer's and Krueger's vaccines given daily and topagen, given in 3 c.c. doses, had no effect. Adult blood-serum, 20 c.c. for infants and 40 c.c. for older children, was successful in 61 per cent of subjects. Hyperimmune serum protected two-thirds of the children and modified the rest. Convalescent serum was the most effective, 15 to 20 c.c. being necessary for an infant and 40 c.c. for an older child.

Curative

Detoxified antigen. N. M. Greenstein and W. Levy gave a toxic filtrate of *H. pertussis*, which had been detoxified with a solution of formaldehyde, to 65 cases of whooping-cough, and arranged for 30 control cases. The dosage was 0.2, 0.4, 0.6, 0.8 and 1.0 c.c., this was later increased to 0.4, 0.6, 0.8, 1.0 and 1.0 c.c. given subcutaneously every other day. Administration of this antigen failed to influence favourably the clinical course of whooping-cough, especially in severe cases and the younger patients. The antigen did not prevent complications of whooping-cough.

M. Weichsel and J. H. Lapin reported the results obtained when an *H. pertussis* antigen which had been detoxified with formalin was used in the treatment and prophylaxis of whooping-cough. A series of 176 children with the disease was treated by injections of 0.3 to 2 c.c. every 2 to 3 days. The average total dose was 4 to 5 c.c. Of these patients 56.3 per cent were benefited by the treatment. Compared with controls, the duration of the disease was shorter and the number of paroxysms was less. To another group of 57 children who had been in contact with whooping-cough 3 to 6 doses of the antigen were given. Of these 37 did not contract the disease, 11 had it mildly, and the remaining 9 had a moderately severe attack. The authors believed that this antigen is useful in the treatment and prevention of whooping-cough, but considered that this series is too small to make definite conclusions.

Ultra-violet irradiation.—P. Delteil and G. Peuteuil reported the use of ultra-violet irradiation in the treatment of whooping-cough. The authors found that ultra-violet irradiation acted as a sort of shock therapy. When the dosage was sufficient to produce agitation, leucopenia, hypertension and mild fever, cure followed very rapidly and the attacks ceased. The first irradiation was from a distance of 90 cm., the second and third from 75 cm.; 4 to 12 irradiations of 3 to 6 minutes were found to be necessary to obtain the desired effect.

Cohen, P., and Lapin, J. (1939) *J. Pediat.*, **15**, 78.

Delteil, P., and Peuteuil, G. (1939) *J. Radiol. Electrol*, **23**, 385.

Greenstein, N. M., and Levy, W. (1940) *Amer. J. Dis. Child*, **59**, 515.

Weichsel, M., and Lapin, J. H. (1940) *Arch. Pediat.*, **57**, 159.

YELLOW FEVER

See also B.E.M.P., Vol. XII, p. 660, and Surveys and Abstracts 1939, pp 145 and 604.

Treatment*Prophylaxis*

Combined yellow fever and smallpox vaccination.— In 1939 Peltier *et al* reported the results of this mixed vaccination in Senegal in 741 persons (see Surveys and Abstracts 1939, p. 605). They now report the results of this mixed vaccination of 100,000 natives of Senegal. As before, the vaccination was carried out by slight scarification of the skin and without bad results. The success of the procedure was shown by serological tests carried out on nearly 1,400 subjects whose blood serum before vaccination was negative, in 95.6 per cent it became positive, in 80.6 per cent strongly so, as regards yellow fever. Growing infants tolerated the treatment well. Serological examination of 47 sailors vaccinated a year before showed that the protection was strong in 46. A hope is expressed that by this mixed vaccination, invasion of Senegal by yellow fever will be prevented. The natives were much impressed by, and their chiefs strongly recommended submission to, the prophylactic vaccination.

Peltier, M., Duneux, C., Jonchère, H., and Arque, E. (1939) *Bull.*

Acad. Med. Paris, **121**, 657.

(1940) *ibid.*, **123**, 137.

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